



Cellular Responses to Stress and Toxic Insults: Adaptation, Injury, and Death

CHAPTER CONTENTS

- Introduction to Pathology 31
- Overview: Cellular Responses to Stress and Noxious Stimuli 32
- Adaptations of Cellular Growth and Differentiation 34
- Hypertrophy 34
 - Mechanisms of Hypertrophy 34
- Hyperplasia 35
 - Physiologic Hyperplasia 36
 - Pathologic Hyperplasia 36
 - Mechanisms of Hyperplasia 36
- Atrophy 36
 - Mechanisms of Atrophy 37
- Metaplasia 37
 - Mechanisms of Metaplasia 38
- Overview of Cell Injury and Cell Death 38
- Causes of Cell Injury 39
- Morphologic Alterations in Cell Injury 40
- Reversible Injury 40
- Necrosis 41
 - Patterns of Tissue Necrosis 43
- Mechanisms of Cell Injury 44
- Depletion of ATP 45
- Mitochondrial Damage 46
- Influx of Calcium and Loss of Calcium Homeostasis 46
- Accumulation of Oxygen-Derived Free Radicals (Oxidative Stress) 47
- Defects in Membrane Permeability 49
- Damage to DNA and Proteins 50
- Clinicopathologic Correlations: Selected Examples of Cell Injury and Necrosis 50
- Ischemic and Hypoxic Injury 50
 - Mechanisms of Ischemic Cell Injury 50
- Ischemia-Reperfusion Injury 51
- Chemical (Toxic) Injury 51
- Apoptosis 52
- Causes of Apoptosis 52
 - Apoptosis in Physiologic Situations 52
 - Apoptosis in Pathologic Conditions 53
- Morphologic and Biochemical Changes in Apoptosis 53
 - Mechanisms of Apoptosis 53
 - The Intrinsic (Mitochondrial) Pathway of Apoptosis 53
 - The Extrinsic (Death Receptor-Initiated) Pathway of Apoptosis 56
 - The Execution Phase of Apoptosis 56
 - Removal of Dead Cells 56
- Clinicopathologic Correlations: Apoptosis in Health and Disease 57
 - Examples of Apoptosis 57
 - Disorders Associated with Dysregulated Apoptosis 58
- Necroptosis 58
- Autophagy 60
- Intracellular Accumulations 61
- Lipids 62
 - Steatosis (Fatty Change) 62
 - Cholesterol and Cholesterol Esters 62
- Proteins 63
- Hyaline Change 63
- Glycogen 63
- Pigments 64
 - Exogenous Pigments 64
 - Endogenous Pigments 64
- Pathologic Calcification 65
- Dystrophic Calcification 65
- Metastatic Calcification 65
- Cellular Aging 66

Introduction to Pathology

Pathology is devoted to the study of the structural, biochemical, and functional changes in cells, tissues, and organs that underlie disease. By the use of molecular, microbiologic, immunologic, and morphologic techniques, pathology attempts to explain the whys and wherefores of the signs and symptoms manifested by patients while providing a rational basis for clinical care and therapy. It thus serves as the bridge between the basic sciences and clinical medicine, and is the scientific foundation for all of

medicine. In chapter 1 we examined the cellular and molecular mechanisms that “define” healthy cells. In this chapter we will build upon that knowledge to discuss the fundamental mechanisms that underlie various forms of cell injury and death.

Traditionally the study of pathology is divided into general pathology and systemic pathology. General pathology is concerned with the common reactions of cells and tissues to injurious stimuli. Such reactions are often not tissue specific: thus acute inflammation in response to bacterial infections produces a very similar reaction in most tissues. On the other hand, systemic pathology examines