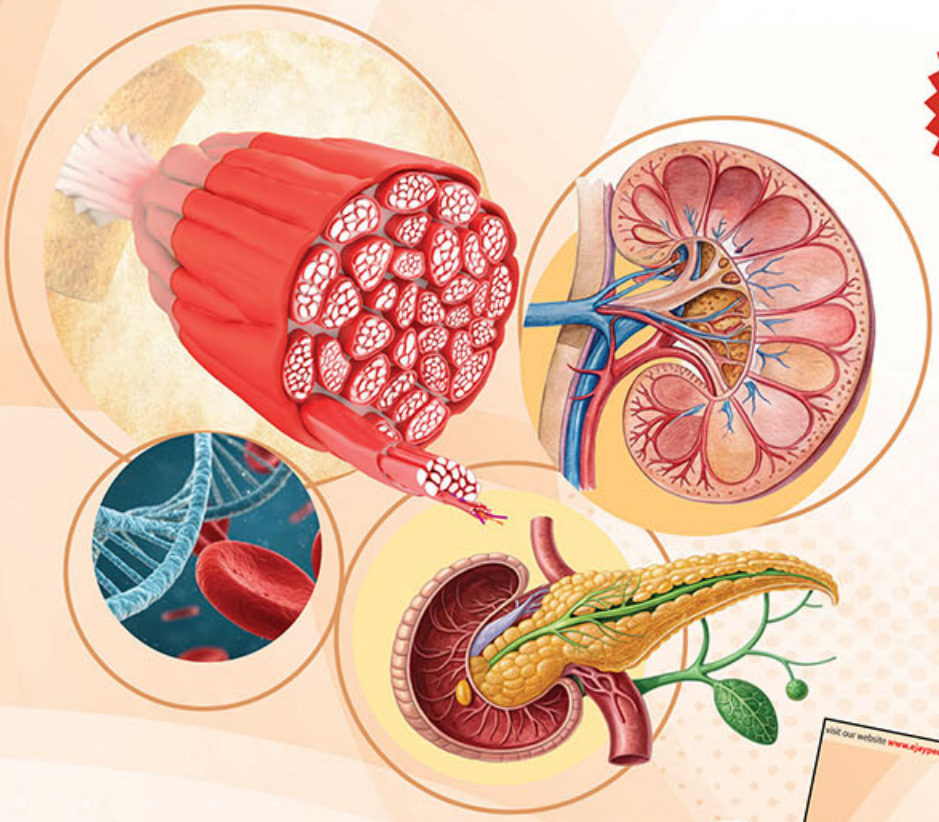
site www.ejaypee.com, for detailed information on physiology books, visit our website www.ejaypee.com, for detailed information on physiology books, visit our website www.ejaypee.com

Dr.Wise
AI Chatbot

Scratch the code inside to access
Dr. Wise your Innovative and Genius AI Chatbot

8th Edition

Free! Practical Manual of Physiology



Pr
PHYS

With Case Scenarios &

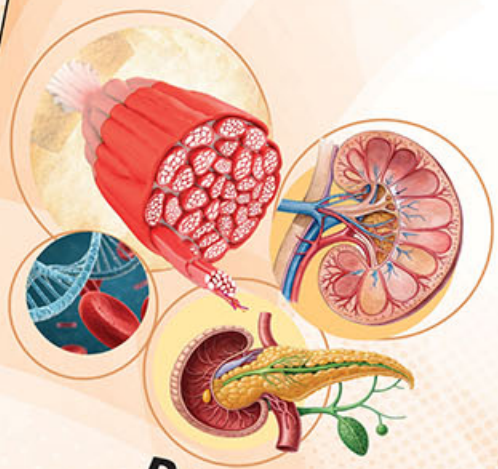
Updated MC

As per the Revised Competency-based

Debasis Pramanik

visit our website www.ejaypee.com, for detailed information on physiology books, visit our website www.ejaypee.com, for detailed information on physiology books, visit our website www.ejaypee.com

8th Edition



Practical Manual of PHYSIOLOGY

A Free Companion to Principles of Physiology, 8/e

As per the Revised Competency-based Medical Education Curriculum (NMC)

Debasis Pramanik

diginerve
A Jaypee Initiative

JAYPEE

Contents

Section 1: General Physiology

1. Structure of a Cell 3
   - Cell Membrane (Fluid Mosaic Model) *3*
   - Nucleus *5*
   - Ribosomes *5*
   - Golgi Apparatus *7*
   - Mitochondria *7*
   - Lysosomes *7*
   - Peroxisomes *7*
   - Filaments *7*
   - Intracellular Motor Proteins or Molecular Motors (Kinesin, Dynein, and Myosin) *8*
   - Intercellular Junctions *9*
   - Gap Junctions *10*
   - Extracellular Matrix (Connective Tissue) and Related Diseases *10*
2. Genes and Protein Synthesis 12
   - Genetic Code *13*
   - Transcription (Synthesis of mRNA) *13*
   - Exon and Intron *14*
   - Translation *14*
   - Post-translational Modification *15*
   - Protein Secretion *15*
   - Regulation of Protein Synthesis *15*
   - Cell Division *16*
   - Cell Cycle *16*
   - Steps of Cell Division *16*
   - Mutation *17*
   - Effects of Mutation on Cell Function *17*
   - Cancer *17*
   - Factors Predisposing to Cancer *18*
   - Oncogenes and Tumor Suppressor Genes *18*
   - Hormones and Cancer *18*
   - Apoptosis *18*
3. Body Fluid Compartments 19
   - Body Fluid Compartments *19*
   - Regulation of Cell Volume *20*
4. Transport Proteins in Cell Membrane 22
   - Water Channel or Aquaporin *22*
   - Ion Channels *22*
   - ATP-dependent Transporters *24*
   - Carriers *24*
5. Transport Across Cell Membranes 25
   - Diffusion *25*
   - Osmosis *27*
   - Effective Osmotic Pressure, Reflection Coefficient, and Tonicity *29*
   - Active Transport *29*
   - Vesicular Transport *32*
   - Homeostasis *32*

Section 2: Nerve Muscle Physiology

6. Resting Membrane Potential 39
   - Cause of the Resting Membrane Potential *39*
   - Donnan Equilibrium *41*
7. Action Potential 42
   - Action Potential and its Ionic Basis *42*
   - Catelectrotonus, Anelectrotonus, and Local Response *44*
   - Refractory Period *45*
   - Threshold Stimulus *45*
   - Strength-duration Curve *45*
   - Rheobase *46*
   - Utilization Time *46*
   - Chronaxie *46*
   - Accommodation *46*
   - All-or-none Law *46*
   - Propagation of Action Potential *46*
   - Saltatory Conduction *47*
   - Compound Action Potential *47*
   - Biphasic Action Potential *47*
   - Injury Potential *48*
   - Effect of Extracellular Ion Concentration on Action Potential *48*
8. Neuromuscular Junction 50
   - Mechanism of Neuromuscular Transmission *51*
   - Difference between Transmission at the Synapse and at the Neuromuscular Junction *52*
   - Agents Affecting Neuromuscular Transmission *52*
   - Myasthenia Gravis *53*
   - Lambert–Eaton Syndrome *54*
   - Denervation Hypersensitivity *54*

9. Mechanism of Muscle Contraction 55
- Skeletal Muscle *55*
- Myofibrils *55*
- Thick Filament *56*
- Thin Filament *56*
- Banding Pattern *57*
- Sarcotubular System *57*
- Excitation-contraction Coupling *58*
- Tetanus and Critical Frequency *60*
- Differences between Cardiac Muscle and Skeletal Muscle *60*
- Differences between Smooth Muscle and Other Types of Muscle *61*

10. Properties of Skeletal Muscle 63
- Types of Muscle *63*
- Length-tension Relationship in Skeletal Muscle *63*
- Chemical Events in Skeletal Muscle *64*
- Phosphorylcreatine *65*
- Aerobic and Anaerobic Glycolysis *65*
- Oxygen Debt *65*
- Motor Unit and Size Principle *66*

Section 3: Hematology

11. Functions of Blood and Blood Volume 73
- Functions of Blood *73*
- Determination of Blood Volume *73*

12. Composition of Blood and Plasma Proteins 75
- Composition of Blood *75*
- Plasma Proteins *75*
- Brief Description of Individual Plasma Protein *76*
- Plasmapheresis *76*
- Function of Plasma Proteins *76*
- Colloidal Osmotic Tension, Starling Hypothesis and Edema *77*
- Edema *78*
- C-reactive Protein *79*

13. The Red Blood Cells 80
- Morphology of Red Blood Cell *80*
- Metabolism of Red Blood Cell *81*
- Function of Red Blood Cell *81*
- Hereditary Spherocytosis and Osmotic Fragility *81*
- The General Scheme of Development of Blood Cells *82*
- Cell Renewal *82*
- Erythropoiesis *82*
- Steps of Erythropoiesis *83*
- Factors Influencing Erythropoiesis *84*
- Pernicious Anemia *85*

14. Hemoglobin 86
- Structure of Hemoglobin *86*
- Synthesis of Hemoglobin *87*
- Fetal Hemoglobin *87*
- Sickle Cell Anemia *87*
- Sickle Cell Trait *88*
- Thalassemia *88*
- Hemoglobin Compounds and Derivatives *88*
- Fate of Hemoglobin *89*
- Anemia *91*
- Anemia due to Blood Loss *92*
- Microcytic Anemia *92*
- Fe-deficiency Anemia *92*
- Aplastic Anemia *92*
- Hemolytic Anemia *92*
- Erythrocyte Sedimentation Rate *92*
- Mechanism of Erythrocyte Sedimentation (Rouleaux Formation) *93*
- Significance of ESR *94*

15. White Blood Cells 95
- Morphological Features of WBCs *95*
- Pools of Neutrophils *96*
- Development of Neutrophils *96*
- Function of White Blood Cell *97*
- Variation in WBC Count and Some Important Clinical Terms *100*
- Reticuloendothelial System or Tissue Macrophage System *100*
- Lymph *100*

16. Platelets and Blood Coagulation 102
- Hemostasis *102*
- Platelets *102*
- Morphological Characteristics of Platelets *102*
- Contents of Platelets *103*
- Functions of Platelets *103*
- Formation of Platelet Plug *103*
- Antithrombotic Role of Aspirin *104*
- Blood Coagulation *104*
- Serum *106*
- Anticlotting Mechanism *107*
- Vitamin K-dependent Clotting Factors *108*
- Anticoagulants *108*
- Tests for Defective Hemostasis *108*
- Coagulation Disorders *109*

17. Blood Group 111
- ABO Blood Group System *111*
- Rh Blood Group *112*
- Grouping and Crossmatching, Universal Donor and Recipient *112*
- Preservation Injuries *113*
- Hazards of Blood Transfusion *113*

- Hemolytic Disease of Newborn *114*
- Importance of Blood Group *114*

18. Immunity 116

- Innate Immunity *116*
- Specific Immunity *117*
- The Lymphoid Tissues in the Body *117*
- Structure of Lymph Node *117*
- B and T Lymphocytes *117*
- Killer or Natural Killer Cells *118*
- Dendritic Cells *118*
- Role of Macrophages in Immunity *118*
- Mast Cells *118*
- Major Histocompatibility Complex Proteins (Human Leukocyte Antigens) *118*
- T Cell Receptor and Immunological Synapse *118*
- Costimulators *119*
- Cell-mediated Immunity *119*
- Activation of B Cells *120*
- General Structure of Immunoglobulins *120*
- The Individual Immunoglobulins *121*
- Genetic Diversity of Immunoglobulins *121*
- Different Actions of Antibodies *121*
- Lymphokines, Cytokines, and Interleukins (The Intercellular Messengers) *121*
- Function of Several Important Interleukins *121*
- The Complement System *122*
- Theories of Immunotolerance *122*
- Theories of Autoimmunity *122*
- Acquired Immunodeficiency Syndrome *123*
- Tissue Transplantation and Graft Rejection *124*

Section 4: Respiratory System

19. Introduction 131

- Types of Respiration *131*
- Anatomical Features of Respiratory Tract *131*
- Structure and Innervation of Tracheobronchial Tree *132*
- Some Features of Pulmonary Circulation *133*
- Effect of Gravity on Pulmonary Circulation *134*
- Pulmonary Vascular Resistance *134*

20. Lung Ventilation 136

- Lung Volumes and Capacities *136*
- Dead Space *138*
- Alveolar Ventilation *139*
- Ventilation-Perfusion Ratio *140*
- Fick's Law of Diffusion *141*

21. Mechanics of Breathing 143

- Intrapleural Pressure *143*
- Pulmonary Pressure *144*
- Changes of the Intrapleural and Intrapulmonary Pressures during Respiration *144*
- Muscles of Respiration *144*
- Sequence of Events Leading to Inspiration and Expiration *145*
- Pressure-volume Relationships *145*
- Compliance *147*
- Surfactant *148*
- Interdependence *150*
- Work of Breathing *150*
- Nature of Airflow and Airway Resistance *150*
- Closing Volume *153*

22. Oxygen Transport 155

- In Physical Solution *156*
- As Oxyhemoglobin *156*
- Oxygen-hemoglobin Dissociation Curve *156*
- Myoglobin *159*

23. Carbon Dioxide Transport 160

- In Physical Solution *160*
- As Carbamino Compounds *160*
- As Bicarbonate *160*

24. Neural Regulation of Respiration 163

- Dual Control of Respiration *163*
- Automatic Control *163*
- Pontine Centers *164*
- Effects of Transection at Different Levels *166*
- Modern Concept of Respiration *166*

25. Chemical Control of Respiration 169

- Short- and Long-term Effect of Hypoxia on Respiration *171*
- Effect of Hypoxia on Ventilation *171*
- Effect of CO_2 on Respiration *172*
- Effect of pH *172*
- Breath Holding *173*
- Voluntary Overbreathing *173*

26. Miscellaneous Topics (Respiration) 174

- Hypoxia *174*
- Carbon Monoxide Poisoning *177*
- Cyanosis *178*
- Asphyxia *178*
- High Altitude Sickness *178*
- Compensatory Changes of Acclimatization *179*
- Alveolar Gas Equation *179*

- Decompression Sickness *180*
- Air Embolism *180*
- Different Types of Breathing *181*
- Effect of Exercise on Respiration *182*
- Artificial Respiration *183*

27. Lung Function Tests 185
- Spirometry Tests *185*
- Anatomical and Physiological Dead Space *185*
- Functional Residual Capacity *185*
- Compliance *186*
- Peak Expiratory Flow Rate *186*
- Diffusing Capacity *186*
- Closing Volume *186*
- Blood Gas and Air Analysis *186*
- Nonrespiratory Functions of Lung *186*

28. Respiratory Diseases 187
- Bronchial Asthma *187*
- Emphysema *187*
- Cystic Fibrosis *188*
- Pneumothorax *188*
- Lung Collapse or Atelectasis *188*

Section 5: Cardiovascular System

29. Functional Anatomy 199
- Circulation through the Heart *199*
- Valves of the Heart *199*
- Pericardium *200*
- Structure of Cardiac Muscle (in Brief) *200*

30. Characteristics of Cardiac Muscle 202
- Properties of Cardiac Muscle *202*
- Electrical Properties *202*
- Mechanical Properties *208*

31. Cardiac Cycle, Venous Waves and Venous Return 215
- Atrial Events *215*
- Ventricular Events *216*
- Factors Controlling Venous Return *218*
- Pressure-volume Loop *219*

32. Cardiac Output 220
- Measurement of Cardiac Output *220*
- Physiological Variations in Cardiac Output *221*
- Factors Controlling Cardiac Output *221*
- Cardiac Function Curve and Vascular Function Curve *224*
- Factors Influencing Cardiac Function Curve *225*
- Factors Influencing Vascular Function Curve *225*
- Integration of Cardiac and Vascular Function Curves *225*
- Canine Heart-lung Preparation *227*

33. Cardiovascular Regulation 229
- Autoregulation *229*
- Circulating Vasoactive Substances *230*
- Innervation of the Heart *231*
- Cardiovascular Centers *232*
- Cardiovascular Reflexes *233*
- Experimental Proofs of Baroreceptor Reflex and Valsalva Maneuver *237*

34. Blood Pressure and its Regulation 238
- Blood Pressure *238*
- Overview of Blood Pressure *238*
- Factors Determining Blood Pressure *239*
- Cardiac Output *239*
- Physiological Variations of Blood Pressure *241*
- Regulation of Blood Pressure *241*
- Effect of Exercise on Blood Pressure *243*
- Hypertension *245*
- Hypotension *245*

35. Heart Rate 246
- Effect of Sympathetic and Parasympathetic Stimulation on Heart Rate *246*
- Physiological Variations in Heart Rate *246*
- Factors Controlling Heart Rate *246*

36. Cerebral Circulation 249
- Special Features of Cerebral Circulation *249*
- Regulation of Cerebral Circulation *250*

37. Coronary Circulation 252
- Special Features of Coronary Circulation *252*
- Factors Regulating Coronary Blood Flow *253*
- Coronary Artery Disease (Myocardial Ischemia and Infarction) *254*

38. Other Circulations 257
- Circulation through Skeletal Muscles *257*
- Regulation of Blood Flow through Skeletal Muscle *257*
- The Microcirculation *258*
- Transcapillary Exchange *258*
- Factors Influencing Microcirculation *258*
- The Fetal Circulation *259*
- Changes after Birth *259*
- Splanchnic Circulation *260*

39. Electrocardiogram 261
- Volume Conduction *261*
- Spread of Cardiac Impulse *261*
- Dipole and Vector *261*
- Convention of Electrocardiography *262*
- The Leads *262*
- Parts of a Normal ECG *264*
- Procedure of Electrocardiography *264*
- Arrhythmias *270*

40. Effect of Gravity and Exercise on Circulation 272
- Effect of Gravity on Circulation *272*
- Postural Hypotension *272*
- Effect of Acceleration and Deceleration *273*
- Effect of Exercise on Cardiovascular System *273*
- Other Integrated Responses during Exercise *274*

41. Hemodynamics 276
- Laminar Flow and Turbulent Flow *276*
- Relation between Velocity of Blood Flow and Diameter of Blood Vessel *277*
- Bernoulli's Principle *277*
- Hagen–Poiseuille Formula *278*
- Relation between Viscosity and Resistance *278*
- Critical Closing Pressure *278*
- Law of Laplace *279*

42. Circulatory Shock 281
- Hypovolemic Shock *281*
- Causes of Irreversible Shock *282*
- Cardiovascular Events in Hemorrhage *283*
- Neurogenic Shock *284*
- Anaphylactic Shock *284*
- Septic Shock *284*

43. Cardiac Failure 285
- Definition *285*
- Causes of Heart Failure *285*
- High Output Failure *285*
- Compensatory Changes in Cardiac Failure [↓ = Decreased; = ↑ Increased] *285*
- Major Manifestations of Decompensated Heart Failure *286*
- Treatment *287*

Section 6: The Digestive System

44. Introduction 299
- Gastrointestinal Tract and Its Functions *299*
- General Anatomical Features of the Gastrointestinal Tract *299*
- Innervation of the Gastrointestinal Tract *300*
- Blood Supply of the Gastrointestinal Tract *300*
- Enteric Nervous System and Gut-Brain Axis *300*

45. Gastrointestinal Hormones 302
- Gastrin *302*
- Zollinger–Ellison Syndrome *303*
- Cholecystokinin-Pancreozymin *303*
- Secretin *303*

46. Salivary Glands and Saliva 304
- Anatomy of the Salivary Glands *304*
- Nerve Supply of Salivary Glands *304*
- Nerve Supply of Salivary Glands *304*
- Constituents of Saliva *305*
- Effect of Rate of Flow of Saliva on its Composition *305*
- Functions of Saliva *305*
- Stimulation of Salivary Secretion *306*
- Control of Salivary Secretion *306*
- Paralytic Secretion *306*

47. The Stomach 307
- Functional Anatomy *307*
- Gastric Glands *307*
- Other Related Cells *308*
- Composition of Gastric Secretion *308*
- Constituents of Gastric Juice *308*
- Mechanism of HCL Secretion *309*
- The Chemical Reactions *309*
- Postprandial Alkaline Tide *310*
- Regulation of HCL Secretion *310*
- Control of Gastric Secretion *311*
- Experiments to Study Gastric Secretion *313*
- Dumping Syndrome *313*
- Functions of Stomach *313*
- Tests of Gastric Function *313*
- Gastric Mucosal Barrier and Peptic Ulcer *314*
- Peptic Ulcer *314*
- Other Factors Causing Peptic Ulcer *314*
- Treatment of Peptic Ulcer *315*

48. Exocrine Pancreas 316
- Main Constituents of Pancreatic Juice *316*
- Control of Pancreatic Secretion *318*
- Steatorrhea *318*
- Acute Pancreatitis *318*

49. The Liver 319
- Anatomical Features *319*
- Composition of Bile *320*
- Constituents of Liver Bile *320*
- Secretion of Bile from Liver *321*

- Control of Bile Secretion *322*
- Enterohepatic Circulation *323*
- Functions of Bile *323*
- Functions of Liver *323*
- Jaundice *323*
- Van Den Bergh Reaction *324*
- Physiological Jaundice *324*
- Difference between Hemolytic and Obstructive Jaundice *324*
- Liver Function Tests *325*
- Gallstones *325*

50. Small Intestine 327
- Brunner's Glands *327*
- Crypts of Lieberkühn *327*
- Villi *327*
- Core of the Villus *327*
- Other Cells in Small Intestine *328*
- Important Constituents of Succus Entericus and their Function *328*
- Regulation of Secretion *328*
- Mechanism of Water and Electrolyte Secretion in Crypts of Lieberkühn *328*
- Movement of Fluid and Electrolyte in Intestine *328*

51. Movements of the Gastrointestinal Tract 330
- Basal Electric Rhythm *330*
- Migrating Motor Complex *331*
- Mastication *331*
- Deglutition *331*
- Achalasia Cardia *332*
- Gastroesophageal Reflux *332*
- Movements of Stomach *332*
- Factors Influencing Gastric Emptying *333*
- Vomiting *334*
- Movements of the Small Intestine *334*
- Segmentation Movements *334*
- Pendular Movements *335*
- Tonic Movements *335*
- Peristalsis *335*
- "Law of Intestine" and "Polarity of the Intestine" *335*
- Gastroileal Reflex *336*
- Paralytic Ileus *336*
- Malabsorption Syndrome *336*
- Steatorrhea *336*
- Movements in the Large Intestine *336*
- Mass Peristalsis *337*
- Defecation *337*
- Gastrocolic Reflex *337*
- Megacolon (Hirschsprung's Disease) *338*
- Dietary Fiber *338*
- Blind Loop Syndrome *338*
- Intestinal Bacteria *338*

52. Digestion 339
- Carbohydrates *339*
- Digestion of Carbohydrate *339*
- Absorption of Carbohydrate *340*
- Lactose Intolerance *340*
- Digestion of Proteins *341*
- The Digestive Process *341*
- Brush Border Proteases *341*
- Absorption of Amino Acids *341*
- Digestion of Fat *341*
- Absorption of Fat *342*

Section 7: Excretory System

53. Nephron 349
- Functions of the Kidney *349*
- Structure of a Nephron *349*
- Bowman's Capsule *350*
- Proximal Convoluted Tubule *351*
- Henle's Loop *351*
- The Distal Tubule *352*
- The Collecting Ducts *352*
- Cortical Nephrons versus Juxtamedullary Nephrons *352*
- Blood Vessels of the Kidney *352*
- Features of Renal Circulation *353*
- Juxtaglomerular Apparatus *353*
- Autoregulation of Renal Blood Flow and Glomerular Filtration Rate *354*
- Renin–Angiotensin System *355*

54. Glomerular Filtration 356
- Factors Influencing Glomerular Filtration Rate *356*
- Glomerular Filtration Rate *357*
- Filtration Fraction *358*
- Determination of Glomerular Filtration Rate *358*
- Criteria of a Substance for Measuring Glomerular Filtration Rate *358*
- Clearance *358*
- Creatinine Clearance *358*
- Renal Blood Flow Measurement by Para-aminohippuric Acid *358*

55. Tubular Reabsorption 360
- Tubular Reabsorption and Transport Maximum *360*
- Different Mechanisms of Na^+ Reabsorption *360*
- Function of the Distal Tubules and Cortical Collecting Duct *364*
- Sodium Balance and Regulation of Extracellular Fluid Volume *364*

- Compensatory Effects in Hypovolemia and Hypervolemia *366*
- Glucose Reabsorption *366*
- Urea Reabsorption *368*

56. Concentration of Urine 369
- The Medullary Osmotic Gradient *369*
- Countercurrent Multiplication *369*
- Role of Urea *370*
- Countercurrent Exchangers *371*
- Concentration of Urine *371*
- Obligatory, Osmotic, and Facultative Reabsorption of Water *372*
- Water Intoxication *373*
- Diuretics *373*
- Osmotic Diuresis *373*
- Sequence of Events in Osmotic Diuresis *374*

57. Regulation of Acid-base Balance 375
- General Principles of Acid-base Balance *375*
- Acid-base Disorder *380*
- Analysis of Metabolic Acidosis *380*
- Evaluation of Acid-base Disorder *381*
- Overview of Acidification of Urine (Summary) *381*

58. Features of Urine 384
- Normal and Abnormal Features of Urine *384*
- Microscopic Constituents of Urine *385*
- Abnormal Constituents of Urine *385*
- Renal Function Tests *386*

59. Micturition 387
- Anatomy of the Bladder *387*
- Nerves of the Bladder *387*
- Pressure Rise in Bladder *388*
- Control of Micturition *388*
- Abnormal Conditions of Bladder *389*

60. The Skin 390
- Types of Skin *390*
- Histological Features *390*
- Appendages of the Skin *391*
- Color of the Skin *391*
- Functions of Skin *392*
- Cutaneous Circulation *392*
- Triple Response *392*

Section 8: Metabolism

61. Enzymes and Carbohydrate Metabolism 401
- Enzymes *401*
- Cofactors and Coenzymes *401*
- Factors Regulating the Rate of Enzyme-Catalyzed Reactions *402*
- Rate-limiting Reaction *402*
- Energy Transfer in Cells and High Energy Compounds *402*
- Hydrogen-accepting Coenzymes *402*
- Oxidative Phosphorylation *402*
- Carbohydrate Metabolism *403*
- Interconversion of Carbohydrate, Fat, and Protein *403*
- Glycolysis (Embden–Meyerhof Pathway) *403*
- Krebs Cycle *405*
- Glycogenesis and Glycogenolysis *405*
- Neoglucogenesis *406*
- Role of Liver in Carbohydrate Metabolism *406*
- Kidney and Blood Glucose Concentration *406*
- Factors Controlling Blood Glucose Level *406*

62. Protein Metabolism 407
- Structure of Proteins *407*
- Transamination and Oxidative Deamination *407*
- Essential Amino Acids *408*
- Urea Synthesis *408*

63. Lipid Metabolism 409
- β-oxidation of Fatty Acids *409*
- Ketone Bodies *410*
- Brown Fat *410*

64. Vitamins and Nutrition 411
- Calorie Requirement of the Body *411*
- Calorie Requirement of Special Groups *412*
- Principles of Preparing a Balanced Diet *412*
- Macronutrients *412*
- Dietary Considerations in Some Special Groups *416*
- Abnormalities of Nutrition *417*
- Cause of Acute Starvation *417*
- Adaptive Changes in the Body in Starvation *417*
- Obesity *418*
- Protein-energy Malnutrition *418*

Section 9: Endocrine System

65. Mechanism of Hormone Action 421
- Classification of Hormones *421*
- Agonist and Antagonist *422*
- Upregulation and Downregulation of Receptors *422*
- G-proteins and Second Messengers *422*
- Mechanisms of Hormone Action *423*
- Feedback Regulation *425*
- Estimation of Hormone Level *426*
- Radioimmunoassay *426*

66. The Pituitary Gland 427
- Anatomical Features of Pituitary Gland 427
- Hypophyseal "Tropic" Hormones 427
- Hypothalamic Releasing Hormones 428
- The Hypophyseal Portal System 428
- Hypothalamus–Pituitary-Target Gland Axis and Feedback Control 428
- Growth Hormone 429
- Factors Influencing Growth Hormone Secretion 429
- Mechanism of Action of Growth Hormone 430
- Actions of Growth Hormone 430
- Somatomedins 431
- Gigantism 432
- Acromegaly 432
- Dwarfism 432
- Pituitary Insufficiency and Sheehan's Syndrome 432
- Thyroid-stimulating Hormone 432
- Adrenocorticotropic Hormone (Corticotropin) 433
- Luteinizing Hormone and Follicle-stimulating Hormone 433
- Prolactin 434
- Actions 434
- Applied 434
- Physiology of Growth 434
- Hormones of Posterior Pituitary 435
- Mode of Action of Vasopressin 435
- Actions of Vasopressin (Antidiuretic Hormone) 435
- Control of Vasopressin Secretion 436
- Applied 436
- Oxytocin 436

67. Thyroid Gland 438
- Structure of Thyroid Gland 438
- Chemistry of Thyroid Hormones 438
- Synthesis of Thyroid Hormones 439
- Mode of Action of Thyroid Hormones 440
- Action of Thyroid Hormones 441
- Regulation of Thyroid Secretion 442
- Features of Hypothyroidism 443
- Myxedema 443
- Causes of Hyperthyroidism 443
- Treatment of Hyperthyroidism 444
- Exophthalmos 444
- Wolff–Chaikoff Effect 444
- Goiter 444
- Thyroid Function Tests 445

68. Adrenal Cortex 446
- Chemical Structure of the Hormones 446
- Biosynthesis of Adrenal Steroid Hormones 447
- Regulation of Glucocorticoid Secretion 448
- Mode of Action of Cortisol (Glucocorticoid) 448
- Actions of Cortisol 448
- Cushing Syndrome 450
- Adrenogenital Syndrome 451
- Aldosterone 452
- Conn Syndrome 453
- Secondary Hyperaldosteronism 453
- Addison Disease 454

69. Adrenal Medulla 455
- Hormones of Adrenal Medulla 455
- Actions of Catecholamines 456
- Effects of Dopamine 457

70. The Calcium-related Hormones 458
- Bone Physiology 458
- Parathyroid Hormone 459
- Parathormone-related Protein 461
- Calcitriol or 1,25-Dihydroxyvitamin D3 461
- Calcitonin 462
- Applied 462
- Tetany 462
- Rickets 463
- Osteomalacia 464
- Osteoporosis 464

71. Endocrine Pancreas 465
- Insulin 465
- Diabetes Mellitus 469
- Complications 470
- Glucagon 471
- Control of Blood Glucose 471
- Effects of Hormones 472
- Effect of Different Organs 472
- Houssay Animal 472
- Glucose Tolerance Test 472
- Hypoglycemia 473
- Pineal Gland 473
- Thymus Gland 474

Section 10: Reproductive System

72. Sex Differentiation 483
- X and Y Chromosome 483
- Development of Gonads and Genitalia 483
- Abnormal Sexual Differentiation 484
- Puberty 485
- Pubertal Changes 486
- Pubertal Abnormalities 486

73. Male Reproductive System 487
- The Male Reproductive Organs 487
- Spermatogenesis 487

- Structure of the Seminiferous Tubule and Blood-testis Barrier *487*
- Stages of Spermatogenesis *488*
- Morphology of a Sperm *489*
- Semen *489*
- Factors Influencing Spermatogenesis *489*
- Testosterone *491*

74. Female Reproductive System 493
- The Female Reproductive Organs *493*
- The Menstrual Cycle *493*
- Folliculogenesis in the Ovary *493*
- Ovarian Cycle with its Hormonal Basis *495*
- Changes in the Uterus—the Menstrual Cycle *497*
- Menstrual Contents *498*
- Changes in the Cervix *498*
- Changes in the Vagina *499*
- Indicators of Ovulation *499*
- Hormones of the Ovary *499*
- Effects of Removal of Gonads *502*

75. Pregnancy and Lactation 503
- Capacitation *503*
- Motility of Sperms *503*
- Fertilization *503*
- Functions of Placenta *504*
- Hormones of the Placenta *504*
- Fetoplacental Unit *505*
- Fetal Graft *506*
- Pregnancy Tests *506*
- Infertility *507*
- Contraception *507*
- Mammary Gland and Lactation *509*
- Effect of Hormones on Breasts *509*
- Secretion and Ejection of Milk *509*
- Effects of Suckling *509*
- Effect of Lactation on Menstruation *509*
- Parturition *510*

Section 11: Nervous System

76. Anatomical Considerations 517
- Anatomy of Brain *517*
- Spinal Cord *518*
- Peripheral Nervous System *518*
- Cranial Nerves *518*
- Anatomy of Spinal Cord *519*
- Cerebrospinal Fluid *520*

77. Neuron 522
- Structure of a Neuron *522*
- Properties of Nerve Fiber *523*
- Axonal Transport *523*
- Neuroglia *523*
- Myelination of Nerve *524*
- Classification of Nerve Fibers *525*
- Neurotrophins *525*
- Nerve Injury—Degeneration and Regeneration *526*
- Changes in Fifth Degree Injury *526*
- Transneuronal Degeneration *527*

78. Synapse 528
- Definition *528*
- Classification of a Synapse *528*
- Structure of a Synapse *528*
- Properties of Synapse *530*

79. Receptor 535
- Definition *535*
- Classification *535*
- Mechanism of Adaptation in Pacinian Corpuscle *537*
- Properties of Receptors *537*

80. Reflex 539
- Definition *539*
- Parts of a Reflex Arc *539*
- Classification of Reflex *539*
- Stretch Reflex *540*
- Structure of a Muscle Spindle *540*
- Innervation *540*
- Action of Muscle Spindle *541*
- Role of γ-Efferents *541*
- Inverse Stretch Reflex *542*
- Clasp-Knife Rigidity *542*
- Other Properties of Reflexes *543*

81. Sensory System 545
- Sensory Areas in Cerebral Cortex *545*
- Disposition of Gray Matter–Rexed Lamina *546*
- White Matter *547*
- Bell–magendie's Law *547*
- Dermatome *547*
- Sensory Coding *547*
- Touch *548*
- Pain Sensation *550*
- Afferent Nerve Fiber of Pain *551*
- Types of Pain *551*
- Pathways of Pain *551*
- Syringomyelia *552*
- Referred Pain *553*
- Dermatomal Rule *553*
- Role of Experience *553*
- Theories Explaining Referred Pain *553*
- Different Instances of "Analgesia" (Loss of Pain Sensation) *553*
- Pain-Inhibiting Mechanisms in the Body *554*
- Thalamic Pain Syndrome *555*

- Surgical Procedures for Relief of Pain *555*
- Hyperalgesia and Allodynia *555*
- Chronic Pain *556*
- Itch Sensation *556*
- Tickle Sensation *556*
- Temperature Sensation *557*
- Spinocerebellar Tracts *557*

82. Motor System **558**
- Overview of Motor System *558*
- Cortical Motor Areas *558*
- Pyramidal Tract *559*
- Extrapyramidal Tracts *560*
- Lower Motor Neuron *561*
- Upper Motor Neuron *561*
- Upper Motor Neuron Lesion versus Lower Motor Neuron Lesion *561*
- Clonus *562*
- Complete Transection of the Spinal Cord *562*
- Features of Brown–Séquard Syndrome or Hemisection of the Spinal Cord *563*
- Tabes Dorsalis *564*

83. Cerebellum **565**
- Anatomical Divisions of the Cerebellum *565*
- Phylogenetic Divisions of the Cerebellum *565*
- Functional Divisions of the Cerebellum *566*
- Afferent Connections of Cerebellum *567*
- Cerebellar Nuclei and their Efferent Connections *567*
- Cerebellar Neurons and Circuitry *568*
- External Connections of the Cerebellum *570*
- Functions *570*
- Signs of Cerebellar Lesion *570*

84. Basal Ganglia **572**
- Anatomy of Basal Ganglia *572*
- Connections of Basal Ganglia *572*
- Functions of Basal Ganglia *573*
- Parkinson's Disease *574*
- Huntington's Chorea *575*
- Wilson's Disease *575*
- Hemiballismus *575*

85. Muscle Tone **577**
- Factors Affecting Integrity of Reflex Arc of Stretch Reflex *578*
- Types of Rigidity *578*

86. Maintenance of Posture and Equilibrium **580**
- Local Static Reflex *580*
- Segmental Static Reflexes *580*
- Tonic Reflexes *581*
- Righting Reflexes *581*
- Hopping and Placing Reflexes *581*
- The Vestibular Apparatus *581*
- The Utricle and the Saccule *581*
- Structure of the Hair Cell *582*
- Semicircular Canals *582*
- Function of the Utricle and The Saccule *583*
- Function of the Semicircular Canals *583*
- Nystagmus *583*

87. Hypothalamus **584**
- Anatomy of Hypothalamus *584*
- Connections of Hypothalamus *584*
- Functions of Hypothalamus *585*
- Temperature Regulation in Detail *588*
- Characteristics of Normal Body Temperature *588*
- Mechanism of Heat Production *588*
- Mechanisms of Heat Loss *589*
- Mechanisms of Temperature Regulation *589*
- Role of Hypothalamus *590*
- Neural Pathway of Temperature Regulation *590*
- Fever *591*
- Hyperthermia and Hypothermia *591*

88. Autonomic Nervous System **592**
- The Parasympathetic Division *592*
- The Sympathetic Division *593*
- Applied *595*

89. Thalamus **596**
- General Considerations *596*
- Thalamic Nuclei *596*
- Connections and Functions of Thalamus *597*
- Reticular Formation *597*
- Reticular Activating System *598*
- Descending Reticular System *598*
- Functions of Reticular Formation *598*

90. Sleep and Electroencephalogram **599**
- Various Rhythms in EEG *599*
- Alpha-Block *599*
- Physiological Basis of EEG Waves *600*
- Patterns of EEG In Sleep *600*
- Genesis of Sleep *601*
- Sleep Cycle *601*
- Usefulness of EEG *602*
- Epilepsy *602*
- Evoked Potential *603*

91. Neurotransmitters **604**
- Receptors of Neurotransmitters *604*
- Reuptake *604*
- Brief Description of Some Individual Neurotransmitters *605*
- Glutamate and Aspartate *606*
- Gaba and Glycine *606*
- Opioid Peptides *606*

- Other Polypeptides *607*
- Cotransmitters *607*

92. Cerebral Cortex 609
- The Cerebral Hemispheres *609*
- Structure of Cerebral Cortex *610*
- Regional Variations in Cerebral Cortex *610*
- Cortical Columns *610*
- The Lobes of the Cerebral Hemisphere *611*
- Cerebral Dominance *612*
- Prosopagnosia *612*

93. The Limbic System 613
- Anatomy *613*
- Connections (Papez Circuit) *613*
- Klüver–Bucy Animal *614*
- Fear and Rage *614*
- Sham Rage *614*
- Areas Involved in Emotion *615*
- Reward and Punishment Systems of the Brain and Motivation *615*

94. Higher Functions 616
- Learning *616*
- Conditioned Reflex *616*
- Memory *617*
- Molecular Mechanism of Memory *617*
- Alzheimer's Disease *618*
- Language *618*

Section 12: Special Sense

95. Structure of the Eye 633
- The Eye *633*
- The Cornea *633*
- The Sclera *633*
- The Middle Coat *634*
- The Iris *634*
- Ciliary Body *634*
- Choroid *634*
- Aqueous Humor *634*
- Glaucoma *634*
- The Crystalline Lens *635*
- Vitreous Humor *635*
- The Retina *635*
- Function of Rods and Cones *637*

96. Optics of the Eye 638
- Accommodation *639*
- Purkinje–Sanson Images *639*
- Presbyopia *639*
- Other Errors of Refraction *639*
- Field of Vision *640*
- Binocular Vision *640*
- Depth Perception *640*

97. Photochemistry 641
- Photochemical Changes in the Retina *641*
- Resynthesis of Photopigments and Role of Vitamin A *642*
- Night Blindness *642*
- Center-surround Antagonism of Receptive Fields *643*

98. Visual Pathway 644
- Anatomy of Visual Pathway *644*
- Vision at Cortical Level *645*

99. Miscellaneous Topics 647
- Color Vision *647*
- Color Blindness *648*
- Purkinje Shift *648*
- Reflexes of the Eye *648*
- Movements of the Eyeball *649*
- Diplopia *649*
- Light Adaptation and Dark Adaptation *650*
- Visual Acuity *650*

100. Hearing 652
- The External Ear *652*
- The Middle Ear *653*
- The Inner Ear *653*
- The Organ of Corti *653*
- The Central Pathways of Auditory Nerve *654*
- Sound Transduction *654*
- Determination of Frequency and Intensity of Sound *656*
- Sound Localization *657*
- Decibels, Sound Intensity, and Hearing Range *657*
- Masking *657*
- Deafness *657*
- Audiometry *658*

101. Taste Sensation 659
- Taste Buds *659*
- Papillae *660*
- Gustatory Papillae *660*
- Mechanical Papillae *660*
- Taste Pathways *660*
- Molecular Mechanism *660*

102. Olfactory Sensation 661
- Olfactory Mucosa *661*
- Olfactory Pathways *661*
- Adaptation of Smell Sensation *662*
- Transduction *662*
- Points to Note *662*
- Pathophysiology of Altered Smell and Taste *663*

Section 13: Advanced Topics

103. Memory 669
- Classification of Memory *669*

104. Smooth Muscle Physiology 673
- Structure *673*
- Excitation-contraction Coupling in Smooth Muscle *673*
- Mechanism of Contraction of Smooth Muscle *674*
- Types of Smooth Muscle *674*
- Stress-relaxation *674*
- Latch Phenomenon *674*
- Detailed Mechanisms of Smooth Muscle Contraction *675*
- Detailed Mechanisms of Smooth Muscle Relaxation *675*

105. Exercise Physiology 677
- Effect of Training in Athletes *677*
- VO_2 Max *677*
- Fatigue after Exercise *678*
- Endurance in Exercise *678*

106. Food Intake and Satiety 679
- Feeding Center and Satiety Center *679*
- Glucostatic Hypothesis *679*
- Role of Arcuate Nucleus *679*
- Leptin and Insulin *680*
- Gut Factors *681*
- Other Factors *681*

107. More about Cerebral Cortex 682
- Motor Cortex *682*
- Sensory Cortex *682*
- Association Areas *683*
- Neuroimaging *683*
- Role of Brain Areas on Emotion in Humans *683*

108. More about Sleep 684
- Function of Sleep *684*
- Role of Neurons in NREM Sleep *684*
- Role of Neurons in REM Sleep *685*
- Hypotonia in REM Sleep *685*

109. Aging, Circadian Rhythm and Space Physiology 686
- Aging *686*
- Circadian Rhythm *687*
- Space Physiology *687*

110. Important Additions I 689
- Mucosal Defense Mechanism in Lung *689*
- The Calcium Clock *690*
- WNK Kinases *690*
- Molecular Mechanism of Apoptosis *691*
- ST Changes in Myocardial Infarction *692*
- Dystrophin *692*
- Regulation of CCK-PZ Secretion *692*
- Aldosterone and ENaCs *692*
- Potassium Channels *692*

111. Important Additions II 694
- Muscular Dystrophies *694*
- Hyperthermic Conditions *694*
- Heat Stroke *694*
- Dialysis and Renal Transplantation *695*
- Reflexes in the Neonates *695*
- Important Developmental Milestones of an Infant *695*
- Indices of Growth and Anthropometry *696*
- Sedentary Lifestyle *696*
- Brain Death *697*
- Meditation *697*

112. Annexure/AETCOM Topics 699

113. Answers to MCQs with Explanation 701

114. Abbreviations 735

115. List of Reference Books 737

Index 739

CHAPTER

81 Sensory System

JAYPEE BROTHERS

LEARNING OBJECTIVES

After reading this chapter, the student should be familiar with:

- ✓ Sensory areas in cerebral cortex 545
- ✓ Disposition of gray matter–Rexed lamina 546
- ✓ White matter 547
- ✓ Bell–Magendie's law 547
- ✓ Dermatome 547
- ✓ Sensory coding 547
- ✓ Physiology of touch sensation 548
- ✓ Pain sensation 550
- ✓ Afferent nerve fiber of pain 551
- ✓ Types of pain 551
- ✓ Pathways of pain 551
- ✓ Syringomyelia 552
- ✓ Referred pain 553
- ✓ Dermatomal rule 553
- ✓ Role of experience 553
- ✓ Theories explaining referred pain 553
- ✓ Different instances of "analgesia" (loss of pain sensation) 553
- ✓ Pain-inhibiting mechanisms in the body 554
- ✓ Thalamic pain syndrome 555
- ✓ Surgical procedures for relief of pain 555
- ✓ Hyperalgesia and allodynia 555
- ✓ Chronic pain 556
- ✓ Itch sensation 556
- ✓ Tickle sensation 556
- ✓ Temperature sensation 557
- ✓ Spinocerebellar tracts 557

SENSORY AREAS IN CEREBRAL CORTEX

1. The sensory receptors situated in the peripheral parts of the body, on being stimulated by various sensory stimuli, transmit impulses along sensory nerves to the spinal cord where they form the ascending tracts **(Fig. 81.1)**.
2. The ascending tracts move upwards along the spinal cord and ultimately reach the cerebral cortex via the thalamus.
3. There are two main areas in the cerebral cortex, which form the sites of termination of the ascending tracts. These are **somatosensory area I** in the postcentral gyrus and **somatosensory area II** in the Sylvian fissure. These are responsible for higher sensory functions **(Fig. 81.2)**.
4. a. Somatic sensory area I (SI) is responsible for sensory processing, such as position sense and discrimination of size and shape.
   b. Somatic sensory area II (SII) is concerned with further processing of sensory information coming to this area from SI.
   c. These two areas perform their functions as if they are connected in series. This is proved by the fact that lesion in SI affects SII function whereas lesion in SII has no effect on SI function.

      (For more detailed information of somatosensory cortex, *see* Chapter 107)
5. The sensory homunculus:
   a. The sensory representation in the postcentral gyrus has a typical pattern.

      The body is represented upside down with the legs above and the head below.
   b. Besides, the area of representation in the cortex of the individual part of the body is proportional to the number of receptors in that part of the body. Diagrammatically, it is shown in **Figure 81.3**, in which each part of the body has been distorted in proportion to its sensory representation in the cortex. This map of sensory representation is known as **sensory homunculus**.
   c. It should be noted that the areas with largest sensory representation (with highest number of receptors) are the thumb and fingers, the lips, parts of mouth, etc.,

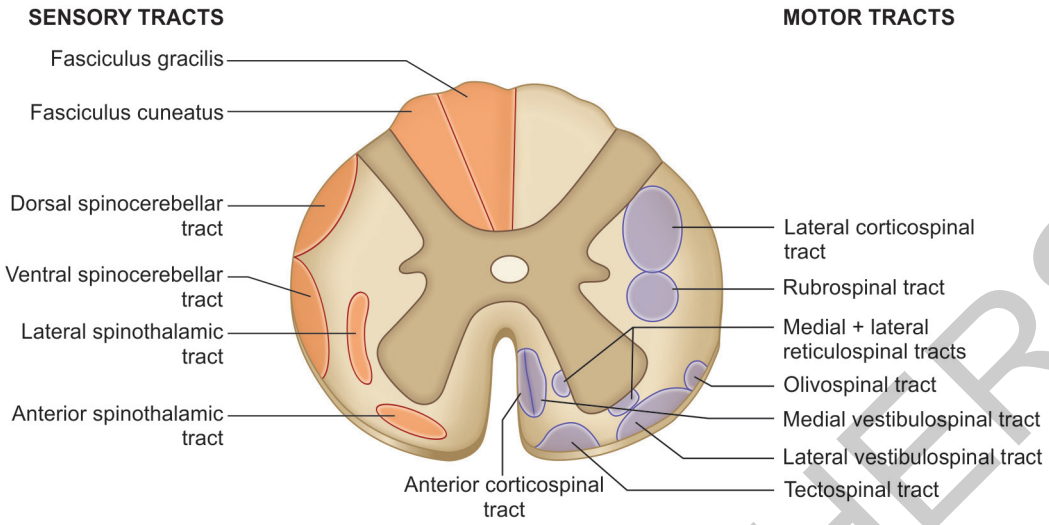


Fig. 81.1: Cross-section of spinal cord showing the sensory (ascending) and motor (descending) tracts.

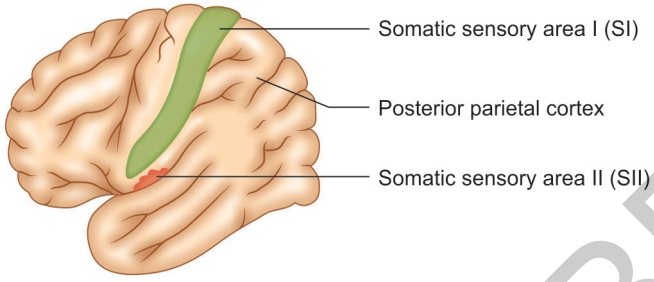


Fig. 81.2: The somatosensory areas of cortex.

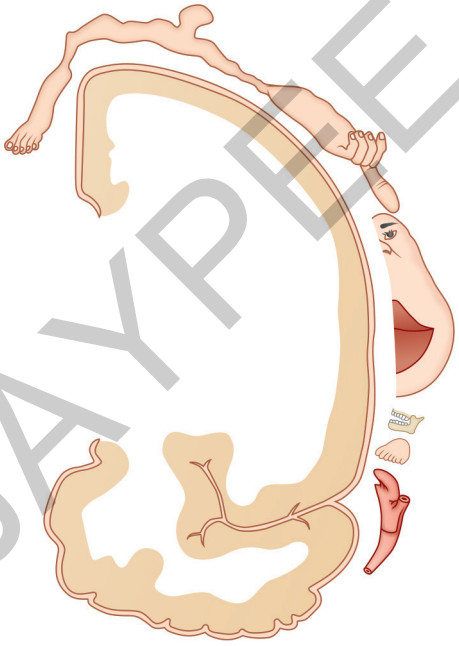


Fig. 81.3: Sensory homunculus. Fingers, thumb, and lip show larger cortical representation.

and so the cortical areas occupied by these parts are disproportionately big.

[**Cortical plasticity**: One may assume from the description of sensory homunculus that sensory fibers from specific parts of the body occupy specific areas of the sensory cortex and this relationship is fixed and immutable.

However, it is seen that in a person with an amputated limb, the cortical area corresponding to the amputated portion is soon occupied by neurons of adjacent portions of the body.

Conversely, if a portion of the cerebral cortex has a lesion or is ablated, the corresponding part of the body is subsequently represented in adjacent cortical areas.

This malleability of cortical representation of body parts is known as cortical plasticity.

This plasticity helps us to explain:

a. The fact that stimulating the amputation stump may cause sensation, which appears to arise in the nonexistent amputated limb. This is an alternative explanation of the **"phantom limb" phenomenon** (*see* p. 537).
b. The observation that a deaf person can have more improved visual function than normal individuals.]

DISPOSITION OF GRAY MATTER–REXED LAMINA (FIG. 81.4)

1. If we consider a cross-section of the spinal cord, we can find that the centrally situated gray matter has the shape of a butterfly, surrounding the central canal and it is divided into anterior, lateral, and posterior horns.
2. Rexed divided the gray matter according to histological pattern into 10 layers or laminae. These are known as Rexed laminae.
3. The posterior horn is divided into laminae I-VI with lamina II and III together constituting substantia gelatinosa of Rolando (SGR).
4. Lamina VII stretches between the anterior and posterior horn while lamina X encircles the central canal.
5. Lamina VIII and IX occupy the anterior horn, lamina VIII being situated medially and lamina IX laterally.

JAYPEE BROTHERS

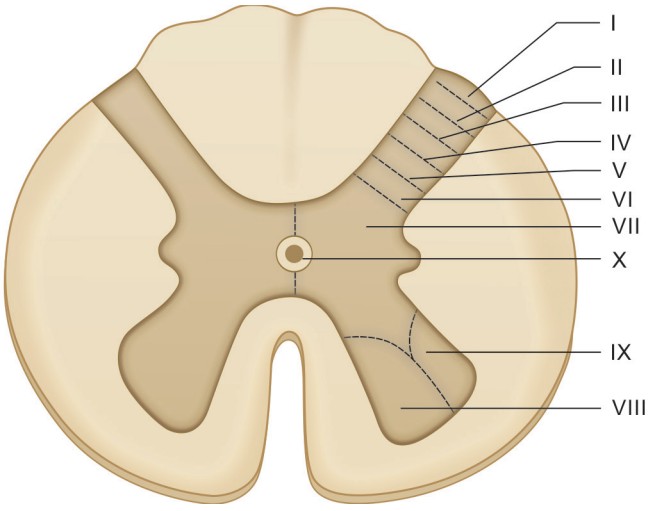


Fig. 81.4: Rexed lamina.

WHITE MATTER

1. In the spinal cord, the butterfly-shaped gray matter divides the surrounding white matter into three funiculi, which are areas of white matter lying in between the horns of gray matter.
2. The anterior funiculus contains the anterior spinothalamic tract. The lateral funiculus contains the lateral spinothalamic tract, the dorsal, and ventral spinocerebellar tracts.
3. The posterior funiculus contains fasciculus gracilis and fasciculus cuneatus (tracts of Goll and Burdach).

BELL–MAGENDIE'S LAW

1. The spinal cord has two nerve roots—(1) anterior (ventral) and (2) posterior (dorsal).
2. The anterior (ventral) root is motor in function as it contains the anterior horn motoneurones (α and γ) along with some preganglionic autonomic fibers.
3. The posterior (dorsal) root is sensory in function as afferent fibers from the periphery (having the nucleus at the dorsal root ganglion) enter the spinal cord through this root.
4. Bell–Magendie's law embodies **the principle that the dorsal root is sensory while the ventral root is motor in function**.

DERMATOME

1. Although the human body is apparently not segmented, the spinal cord is functionally divided into distinct segments. In embryonic life, the body was likewise distinctly segmented. So, the tissues, the muscles, and the nerves all follow a specific segmental pattern as they develop from the same embryonic segment.
2. **Portion of the skin, supplied by nerves from one such segment of spinal cord, is known as dermatome**. Dermatomes, especially in the limbs, may have apparently irregular shape because of the manner in which the upper and lower limbs have projected out from the trunk. Another contributing factor is the upright posture of the humans. However, **when a person adopts the posture of a quadruped, these so-called irregular dermatomes become aligned in a distinctly segmented pattern**.
3. There is some degree of overlap in the nerve supply of a dermatome and it receives additional supply from collaterals of nerves in adjacent dermatomes. This explains the near absence of sensory loss when a single dorsal nerve root is transected. Several contiguous nerve roots have to be transected in order to produce anesthesia in a single dermatome.

SENSORY CODING

Sensory coding involves mode of transmission of information related to different properties of a sensory stimulus. These properties include modality, location, intensity, frequency and duration of the stimulus.

- **Modality** of a stimulus signifies the nature of stimulus such as touch, pain, temperature, etc. This may be encoded by a "labeled line principle" as elucidated by **doctrine of specific nerve energies** (p. 537) in which the modality of sensation is determined by the termination of neurons carrying the sensation in specific parts of sensory cortex.

  Modality may also be determined by stimulus frequency. Thus, a low frequency mechanical stimulation conveys touch sensation whereas a higher frequency mechanical stimulus conveys vibration sense.

  Modality is also indicated by the **property of adequate stimulus of the involved receptor**. For example, when the modality or stimulus type is vision, it is encoded by photoreceptors which are stimulated with activation of their specific transduction mechanisms and the adequate stimulus of these receptors is light. From this, the sensory system can recognize the modality or stimulus type.
- **Location** of the stimulus is encoded by the anatomical distribution of receptive fields of the activated receptors. Collectively, these receptive fields can form anatomical maps such as somatotopic maps represented in the sensory cortex.

  The labeled line principle, mentioned above, of action potential transmission not only indicates modality or stimulus type but also they give information about the **exact location of the activating stimulus through the receptor (Law of projection)**.

  Punctate distribution of receptors lying discretely on the skin and specifically activating particular stimulus type, also helps localize the exact site of stimulation.

  Two more properties of receptors also contribute to determination of the exact location of the sensory stimulus.

JAYPEE BROTHERS

One is **2-point discrimination** (vide supra) by which the sensory system can recognize two closely located stimuli separately.

The other principle is **lateral inhibition** (p. 538) which also helps in pinpointing the exact location of stimulus.

- **Intensity** is encoded by **frequency of transmitted action potentials and also by the number of neurons stimulated**. This can also be encoded by stimulation of particular sets of receptors with different thresholds. Thus low threshold receptors may convey lower intensity whereas high threshold receptors may convey higher intensity. Together they can respond to a widened range of intensity which is very useful.
- **Frequency** of the stimulus is encoded by the time intervals between successive action potentials. Sometimes, these interspike intervals match exactly with frequency of the stimulus (as seen in **the volley principle** of transmission by auditory neurons in the low frequency hearing range).
- **Duration** of the stimulus is encoded by the property of adaptation (vide supra) seen in slowly adapting and rapidly adapting type of receptors. The slowly adapting or nonadapting receptors encode the length of stimulus duration whereas rapidly adapting receptors encode the initiation and termination of stimulus duration.

TOUCH

Receptors

1. **Slowly adapting**—Merkel's disks, Ruffini end-organs, etc.
2. **Rapidly adapting**—Pacinian corpuscles, Meissner's corpuscles, etc. Receptors around the hair follicle are also important receptors of touch.

Merkel's disk and Meissner's corpuscle are present superficially on the surface of the skin whereas Ruffini end-organs and Pacinian corpuscles are present in relatively deeper layers of skin.

Pacinian corpuscles and Meissner's corpuscles, due to their rapidly adapting nature, detect rapid changes like vibration sensation.

Pacinian corpuscles respond to high frequency (300 Hz) vibration whereas Meissner's corpuscle, found exclusively in glabrous (nonhairy) skin, respond to low frequency vibration of 50 Hz. Hair follicle receptors are found only in hairy skin whereas the other three touch receptors, e.g., Pacinian corpuscle, Ruffini end-organs, and Merkel's disk, are found in both hairy and glabrous skin.

A number of Merkel's disks are sometimes present as a group, producing a dome-shaped elevation protruding from the skin. They are connected to a single large diameter afferent nerve and they are known as **Iggo dome receptor**. They help in localizing touch and assessing texture.

Transduction of touch is an area of intense research. While previous studies postulated ASIC (acid-sensing ion channel) as the likely mediator of touch sensation, knockout studies involving ASIC could not prove it.

More recent studies, however, have shown that a non-selective cation channel present in dorsal root ganglion cells called **Piezo2** probably mediates rapidly adapting touch sensation as well as some degree of visceral sense and proprioception.

Afferent Nerves

Touch is carried by Aβ fibers having a diameter of 5–12 μm with a high conduction velocity of 30–70 m/second. Some C fibers also carry touch sensation.

Relation between Touch Afferents and Touch Receptors

Touch afferents may arise from rapidly adapting (RA) or slowly adapting (SA) low threshold mechanoceptors (touch receptors). Again, they may innervate small receptor fields with well-defined borders (Type 1) or their receptive fields may be much wider with ill-defined borders (Type 2).

Accordingly, these low threshold touch afferents may be grouped into four classes (RA1, RA2, SA1 and SA2). RAI and RA2 are also called FA1 and FA2 (fast adapting).

In glabrous or non-hairy skin, RA1 and SA1 afferents innervate Meissner's corpuscle and Merkel's disk respectively, which are located superficially or just below the epidermis with small receptive fields.

On the other hand, RA2 and SA2 afferents innervate Pacinian corpuscles and Ruffini endings respectively, both lying deeper in the dermis. Their deeper location explains their relatively large receptive fields.

In hairy skin, SA1 and SA2 afferents connected to Merkel cells and Ruffini endings respectively are present. RA2 afferents are connected to Pacinian corpuscles which are present in much deeper tissues whereas true RA1 afferent is absent.

However, the hairy skin contains afferents called hair units which may innervate up to 20 hairs. They surround the hair follicles and are extremely sensitive to touch.

Pathway (Figs. 81.5A and B)

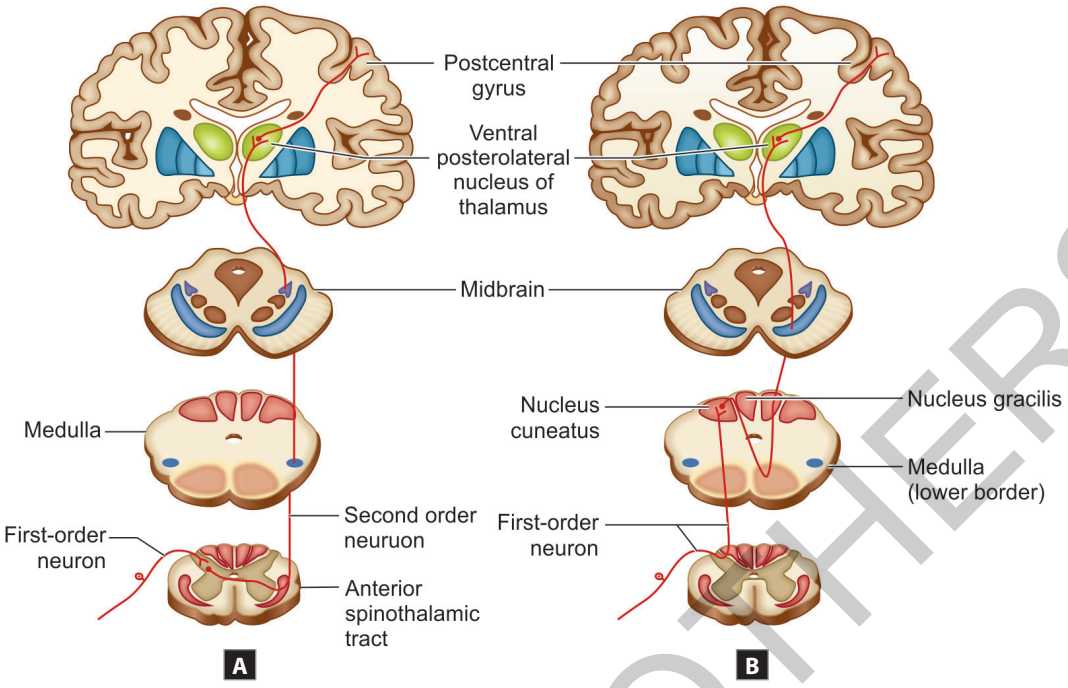
Touch is carried through:

1. The dorsal columns consisting of the tracts of Goll and Burdach. These are also called the lemniscal system.
2. The anterior spinothalamic tract.
3. The trigeminal nerve which transmits touch sensation from the face.

A. Dorsal column or lemniscal system:
(Tracts of Goll and Burdach):

1. The sensory impulses concerned with—(1) fine touch, (2) tactile localization, (3) vibration sense and (4) proprioception are carried to the cerebral cortex via the dorsal columns.

JAYPEE BROTHERS



Figs. 81.5A and B: Pathway of touch. (A) The anterior spinothalamic tract carrying crude touch; (B) Dorsal column pathway conveying fine touch.

Note: Conscious proprioceptive sense is carried by dorsal column. Although most of the fibers carrying proprioceptive sense end in cerebellum, some pass to the cortex via the thalamus.

These latter fibers are believed to carry sensation of conscious proprioception.

Conscious perception of the outline of body image is created from the combined sensory inputs of—(1) slowly adapting spray endings located around joints, (2) Pacinian corpuscles, (3) touch receptors, and (4) muscle spindles.

2. The first-order neurons arising from the periphery and carrying touch sensation have their cell body in dorsal root ganglion. They have unusually long axons which move up along the ipsilateral dorsal column after entering the spinal cord and end in the nucleus gracilis and nucleus cuneatus near the junction between the medulla and spinal cord to relay with the second order neurons. Some fibers end in an accessory cuneate nucleus.
3. The nerve fibers coming from the lower part of the body form the fasciculus gracilis **(tract of Goll)**. Fibers coming from upper segments gradually push these fibers to the medial side. Fibers from the upper part of the body (above midthoracic level) form the fasciculus cuneatus **(tract of Burdach)**.
4. Second-order neurons arise from the nucleus gracilis and nucleus cuneatus. These are called **internal arcuate fibers**.

   They cross immediately to the opposite side and move upwards as the **medial lemniscus** to end in the **ventral posterolateral (VPL)** nucleus of the thalamus.
5. Some fibers known as **posterior external arcuate fibers**, arising from the accessory cuneate nucleus, pass ipsilaterally ending in cerebellum. They are responsible for unconscious proprioception.
6. Third-order neurons arise from the thalamus and ascend via the posterior limb of the internal capsule and end in the sensory cortex (postcentral gyrus).

B. Anterior spinothalamic tract:

1. Sensory impulses concerned with crude touch pass from the periphery via first order neurons having the cell body in the dorsal root ganglion.
2. These fibers have short axons which end in the posterior horn of the spinal cord where the second order neurons arise. They cross to the opposite side in front of the spinal canal and ascend in the anterior funiculus as the anterior spinothalamic tract. This tract ultimately ends in the VPL nucleus in the thalamus.
3. Third-order neurons arise from the thalamus and end in the postcentral gyrus after passing through the posterior limb of the internal capsule.

C. Trigeminal nerve (Fig. 81.6):

1. Touch sensation from the face region is carried via the trigeminal nerve. The cell body of the first-order neuron lies in the trigeminal ganglion.
2. The second-order neuron arises from the principal sensory nucleus in the pons, crosses to the opposite side, and ends in the **ventral posteromedial (VPM)** nucleus of the thalamus.
3. Third-order neurons arise from the thalamus, pass through the posterior limb of the internal capsule, and end in the postcentral gyrus.

JAYPEE BROTHERS

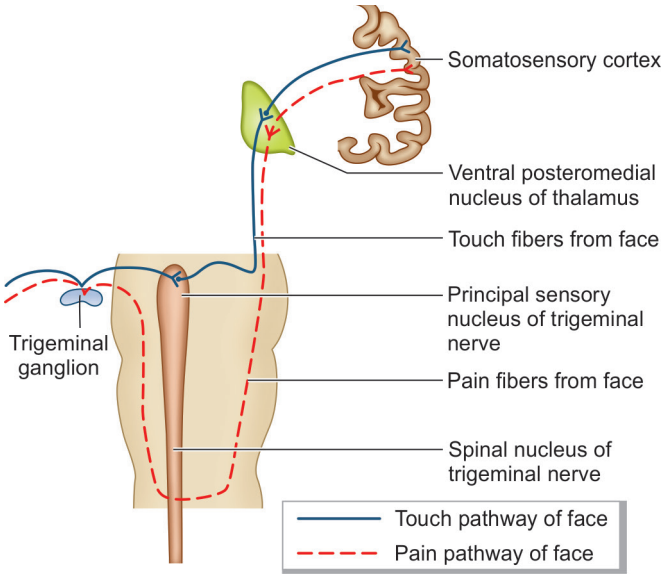


Fig. 81.6: Schematic diagram of pathways of touch and pain from face.

Medial lemniscus is formed by second-order neurons of tracts of Goll and Burdach.

Spinal lemniscus is formed by ascending second-order neurons of lateral spinothalamic tract carrying pain and temperature sensation.

Trigeminal lemniscus is formed by second-order neurons of sensory part of trigeminal nerve.

Lateral lemniscus is a part of auditory pathway.

Some higher sensory functions (requiring the cortex for perception) associated with touch are:

1. **Stereognosis:** It is the ability to identify an object by assessing the size, shape, texture, and weight of the object while keeping the eyes closed.
2. **Two point discrimination:**
   a. If two points are situated very close to each other, it may be impossible to discriminate between them when they are stimulated simultaneously.
   b. The minimum distance that should separate two points, at which even on simultaneous stimulation they can be discriminated as separate points, is known as "minimum separable", or two-point touch threshold.
   c. Two-point touch threshold varies inversely as the density of receptors. For example, in the fingertips with high receptor density, it is only a few mm, whereas, in the back with low receptor density, it is quite large.
3. **Tactile localization:** Although the eyes are closed, the subject can almost accurately localize the point on the body stimulated by touch. This is known as tactile localization.

Note: Blind persons can "read" Braille symbols, which are raised dots separated by a distance of 2.5 mm which is a little greater than "two-point touch threshold" at the fingertips. This enables the blind person to discriminate between adjacent dots and decipher the symbols.

4. **Graphesthesia:** If a number or letter is written by a finger on the palm or on the back of a subject, the subject is able to recognize the number or letter even when the eyes are closed. This ability is known as graphesthesia.
5. **Texture of an object:** Keeping the eyes closed, we can easily identify objects made of paper, cloth, metal, or wood. This ability to recognize the texture of the object, though linked to touch, is integrated in the cerebral cortex.

PAIN SENSATION

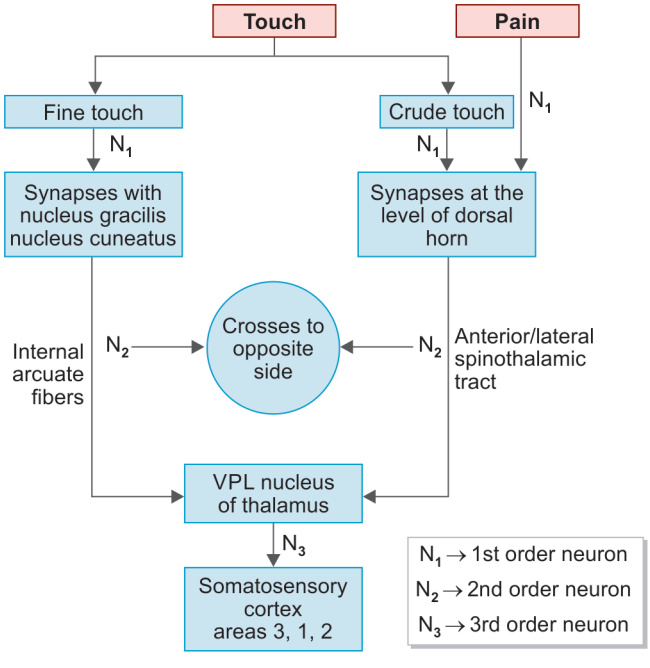
Pain is an unpleasant sensation associated with tissue damage. It warns the body about imminent damage and so it has protective function. That is why Sherrington aptly termed it as **"physical adjunct of an imperative protective reflex" (Flowchart 81.1)**.

Receptor

Pain sensation arises from free nerve endings which are called nociceptors. The nociceptors are divided into several types according to their function. Thus, mechanical nociceptors sense pressure changes in the skin, chemosensitive nociceptors respond to chemical agents like histamine, bradykinin, etc., whereas thermal nociceptors are stimulated by raised temperature and extreme cold. Polymodal nociceptors sense more than one of these stimuli.

The free nerve endings, i.e., the nociceptors, again contain receptors which are activated by various stimuli. Thus, TRPV1 receptors sense intense heat, acids, and presence of capsaicin (which is a vanilloid chemical). These receptors belong to the family of **transient receptor potential (TRP) channels** (*see* p. 23).

Flowchart 81.1: Schematic representation of ascending tracts carrying touch and pain (sensory pathways from face and paleospinothalamic pathway of pain are excluded).



JAYPEE BROTHERS

The TRPA1 receptors are activated by painful mechanical, chemical, and cold stimuli. TRPV2 receptors sense intense heat in the range of 60°C.

Noxious heat or noxious cold is caused by temperatures >43°C and <15°C respectively.

Some receptors are indirectly activated by various stimuli through intermediary agents. Thus, **purinergic pain receptors** (P2X and P2Y) are stimulated by ATP which is secreted in response to painful mechanical stimuli.

Other pain receptors are stimulated by immune intermediaries such as bradykinin, prostaglandin, and cytokines. Thus, these receptors are activated by tissue injury and they sense pain due to inflammation.

A **tetrodotoxin-resistant Na^+ channel** plays an important role in pain perception in humans. This is proved by the fact that a genetic mutation involving this channel is found in individuals who are totally incapable of feeling pain.

AFFERENT NERVE FIBER OF PAIN

1. Aδ type of nerve fiber carries fast pain.
2. C type of nerve fiber carries slow pain.

TYPES OF PAIN

1. Pain is of two types—(1) **fast pain** and (2) **slow pain**. These are also known as "first pain" and "second pain" respectively.
2. When a tissue is incised by a sharp instrument, say, a knife, there is an immediate, sharply localized pain felt at the area. This is known as fast pain.

   It is transmitted via Aδ fibers, having a higher velocity of conduction.
3. The "fast" pain is followed by a dull, diffuse, and burning type of pain. This is the "slow" pain and is transmitted by the slowly conducting C fibers.
4. Increase in the distance between the site of application of the painful stimulus and the brain, increases the time interval separating the two types of pain felt. This proves the separate conduction velocities of the "fast" and "slow" components of pain.
5. Newer nomenclature has replaced the terms fast pain and slow pain by the use of such terms as "discriminative" pain and "motivational-affective" pain. Fast pain which senses **localization and intensity**, ultimately stimulates somatosensory cortex and this is called **"discriminative"** pain.

   In contrast, slow pain pathways activating brainstem reticular formation and centrolateral nucleus of thalamus and ending in widespread areas of brain, such as cingulate gyrus, amygdala, frontal lobe and insular cortex, are concerned with **emotional or affective** component of pain. Hence, this type of pain is termed **"motivational-affective"** pain.

PATHWAYS OF PAIN (FIG. 81.7)

1. The first-order neuron of pain pathway arises from the receptors, i.e., free nerve endings and runs toward the spinal cord.
2. There are two different types of fibers, as already mentioned:
   a. The Aδ fiber is of larger diameter (2–5 μm) and has a higher conduction velocity (12–30 m/s).
   b. In contrast, the C fibers are smaller (0.4–1.2 μm in diameter) with a conduction velocity of 0.5–2 m/s.

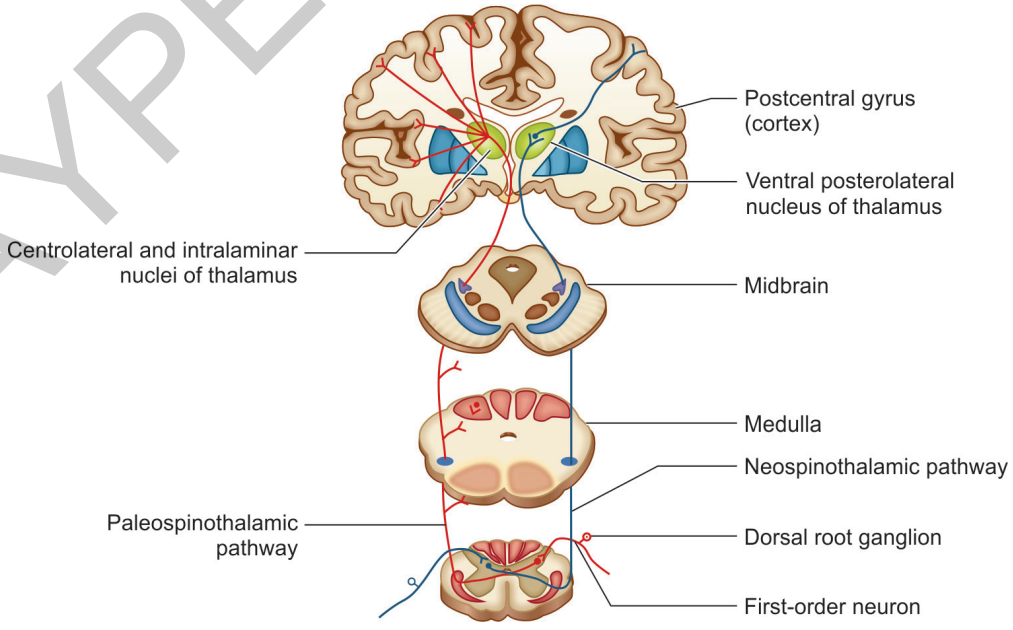


Fig. 81.7: Pathway of pain: The right half shows the neospinothalamic pathway. The left half shows the paleospinothalamic pathway.

JAYPEE BROTHERS

3. Both types of fibers end in the posterior horn. The Aδ fibers end in lamina I, V and X (of Rexed) whereas C fibers terminate in lamina I and II. The nerve fibers may move up or down a few segments before terminating in the dorsal horn, thereby forming the tract of Lissauer.
4. The pathway formed by Aδ fibers is known as **neospinothalamic pathway** and the neurotransmitter secreted is believed to be glutamate.
5. On the other hand, the pathway formed by C fibers is called the **paleospinothalamic pathway** and its neurotransmitter is probably substance P. CGRP is another peptide also released at the same site, which prevents degradation of substance P and enhances its action.

It should be noted that some second order neurons receive input from touch receptors in addition to receiving pain stimuli. These are called wide dynamic range cells signifying their sensitivity to both mechanosensitive stimulus (touch) as well as pain sensation, with the two types varying in intensity.

6. Neospinothalamic pathway:
   a. The second-order neuron arises from the posterior horn, crosses to the opposite side in front of the central canal, and ascends in the lateral funiculus as the lateral spinothalamic tract.

      The fibers of the lateral spinothalamic tract in the upper segments of the spinal cord, on reaching the lateral funiculus, push the ascending fibers from the lower segments laterally toward the surface. Therefore, the lateral spinothalamic tract is laminated and the fibers from the sacral, lumbar, thoracic, and cervical segments are arranged in a lateral to medial direction in the lateral funiculus.

      So, an intraspinal tumor will affect pain sensation in the upper segments first whereas an extraspinal tumor will affect pain sensation in the lower segments first.
   b. The lateral spinothalamic tract terminates in the **VPL nucleus of the thalamus**.
   c. From there, third order neuron arises, passes through the posterior limb of the internal capsule, and ends in the postcentral gyrus.
7. Paleospinothalamic pathway:
   a. This pathway is somewhat different. One or more short neurons may be interposed between the first-order neuron and the neuron crossing to the opposite side and ascending in the lateral funiculus.
   b. **Only 10–25%** of the long ascending neurons end in the thalamus.
   c. The rest may end in:
      - The reticular formation of the brainstem.
      - The tectal area of the midbrain deep to the superior and inferior colliculus.
      - The periaqueductal gray (PAG) (p. 555).
   d. From the brainstem, neurons may proceed to centrolateral and intralaminar nuclei of thalamus. Other nerve fibers go to certain areas of hypothalamus and also to areas of basal brain. Fibers also end in cingulate gyrus, mediofrontal, and insular cortex.
   e. The diffuse connections of the paleospinothalamic tract explain the poorly localized type of slow pain perceived by it.
   f. Convergent afferent input from viscera to these pain-carrying spinothalamic fibers explain the phenomenon of referred pain as explained later (*see* below).
   g. The second order neurons ascending in the paleospinothalamic pathway and terminating in the reticular formation and midbrain have also been named as spinoreticular and spinomesencephalic tracts respectively.
   h. It should also be noted that fibers going to the cingulate gyrus and insula are involved with affective (emotional) responses. Neurons from midbrain also go to amygdala to mediate similar emotional responses.
8. **Pain sensation from the face** is carried by trigeminal nerve. The axons of the first-order neurons end in the spinal nucleus of the trigeminal nerve. Second-order neurons arise from the spinal nucleus and cross to the opposite side to end in the **VPM nucleus** of the thalamus.

   From this, the third-order neuron arises and passes through the posterior limb of internal capsule to end in the postcentral gyrus **(Fig. 81.6)**.
9. Destruction of VPL and VPM nuclei abolishes only sensory-discriminative type of pain but an intact medial part of thalamus is associated with persistence of motivational-affective type of pain. This provides a proof of the different pathways used by the two types of pain.
10. Thalamic pain, a severe type of pain in a thalamic lesion, can be evoked by even a mild touch stimulus. This has a central origin (not caused by stimulation from periphery) and is probably caused by invasion of undamaged thalamic neurons by sprouting touch fibers.

Although pain fibers end in the cortex which senses the finer aspects of pain, pain can also be sensed at a subcortical level, e.g., at the thalamus. In cortical lesion, pain perception is the least affected sensory modality as it is perceived at the thalamic level to a large extent.

Of the other types of sensations, temperature sensation is affected to an intermediate degree in cortical lesion while fine touch and proprioception are most severely affected.

SYRINGOMYELIA

1. In this disease, the area in front of the central canal in the spinal cord is affected by gliosis and cavity formation. This disrupts the anterior and lateral spinothalamic tracts which cross in front of the central canal (in the anterior commissure).
2. So, pain, temperature, and crude touch sensations are lost as the lateral spinothalamic tract carries pain and temperature sensation whereas anterior spinothalamic tract carries sensation of crude touch.

JAYPEE BROTHERS

However, fine touch persists as it passes via the ipsilateral dorsal column, i.e., tracts of Goll and Burdach. This condition, therefore, is said to exhibit dissociated sensory loss or **"dissociated anesthesia"** which is pathognomonic of this disease.

REFERRED PAIN

1. Irritation in deeper structures, especially in the viscera, produces pain which is felt in a superficial somatic area remote from the affected site. This is called referred pain.
2. Referred pain is of great clinical importance because a good knowledge of the sites of referred pain provides the clinician or surgeon with important clues for diagnosing many diseases.
3. A typical example is pain from an inflamed gallbladder irritating the diaphragm being referred to the right side of the neck or cardiac pain being referred to the inner aspect of left arm.

DERMATOMAL RULE

1. Pain is not referred at random. It is referred to an area or dermatome which develops from the same embryonic segment as that of the affected viscera or organ. This is called dermatomal rule.
2. For example:
   a. We know that pain sensation arising from the diaphragm is referred to the neck. The diaphragm and the area of neck where the pain is referred, arise from the same embryonic segments and both are supplied by phrenic nerve (C_3, C_4, and C_5).
   b. Similarly, pain sensation arising from the heart is referred to the inner aspect of left arm. Now, the heart and inner aspect of left arm both arise from the same embryonic segment.
   c. Also, pain in the ureter is referred to the testis and both ureter and testis have a common segmental origin.

ROLE OF EXPERIENCE

1. Areas with previous experience of trauma may sometimes be the sites of referred pain. For example, pain due to operation in maxillary sinus may be referred to distant sites where dental operations were performed previously.
2. Similarly, the pain due to acute appendicitis, which is usually referred around the umbilicus, may be referred to the site of abdominal scar of a previously performed surgical operation.

THEORIES EXPLAINING REFERRED PAIN (FIG. 81.8)

1. **Convergence theory:**
   a. According to this theory, afferent nerve fibers carrying pain sensation from the affected viscera as well as those coming from the referred site **converge on a common second-order neuron.** (As the total number of second order neurons is less than that of first-order neurons, this is only to be expected).
   b. Now, when stimulation of pain receptors in the viscera leads to transmission of impulses to the cerebral cortex, it is interpreted by the brain as coming from the referred "somatic" site which is commonly involved in different painful stimuli.
   c. The site of convergence is believed to be in lamina I-VI of Rexed. However, afferent nerves from both sides converge at lamina VII and this explains how pain originating in viscera of one side may be referred to a site on the opposite side.
2. **Facilitation theory:** According to this theory, impulses carrying pain sensations in the afferent neurons from the viscera have a **subliminal fringe effect** on the dorsal horn synapses of somatic afferent neurons carrying pain sensation from the referred site. As a result, pain stimulus of very low intensity in the somatic afferents will be potentiated by visceral pain and conveyed to the brain to evoke pain sensation.

   It is observed that anesthesia of the superficial somatic site reduces the intensity of referred pain. So, an afferent input from the peripheral somatic site must be active in causing referred pain. This supports the facilitation theory.

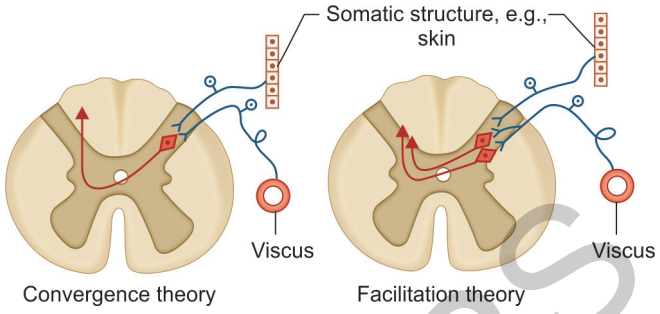


Fig. 81.8: Convergence and facilitation theories of referred pain. (see text for explanation)

DIFFERENT INSTANCES OF "ANALGESIA" (LOSS OF PAIN SENSATION)

Stress Analgesia

Stressful conditions may cause temporary analgesia (absence of pain sensation). For example, a soldier may be severely wounded in a battle, but in presence of the excitement and stress, he may feel no pain at all during the period of stress.

However, he feels severe pain as the "heat" or stress of battle is over. This type of painless condition during stress is known as stress analgesia.

Several factors are believed to contribute to stress analgesia. These are:

- It is mediated by **endocannabinoids** 2-arachidonylglycerol and anandamide. These act via CB_1 and CB_2

JAYPEE BROTHERS

receptors. Agonists of CB_2 receptor have been found to cause analgesia.

- ❖ Norepinephrine secreted from catecholaminergic neurons acts on amygdala and modulates motivational-affective component of pain via amygdala. Thus, it helps in producing stress analgesia.
- ❖ Opioids are also believed to play a role in stress analgesia as it is partially reduced by administration of opioid antagonists such as naloxone.

Analgesia may also be caused by counter irritants, local rubbing, or acupuncture. In China, acupuncture has been in vogue from ancient times for relief of pain.

Surgical procedures have been successfully carried out under acupuncture anesthesia.

The above facts point to some pain-inhibiting mechanisms in the body described below.

PAIN-INHIBITING MECHANISMS IN THE BODY

1. **Gate-control theory:**
   a. It is a complicated theory. Simply stated, the large diameter afferent fibers, e.g., Aβ touch fibers of the dorsal column give recurrent collaterals which end on pain afferents directly or through an inhibitory interneuron working like a gate.
   b. Local rubbing at the site of pain activates touch fibers which ascend through the dorsal horn lying close to the pain afferents. At the level of dorsal horn, recurrent collaterals from the large diameter touch fibers end on the pain afferents either directly or through an interneuron. This ultimately causes presynaptic inhibition of the pain afferent, decreasing pain transmission like a gate. As a result, no impulse can pass through the pain afferents, causing analgesia (the gate is closed). The outline of the original theory is as follows **(Fig. 81.9)**:
      - ♦ According to this theory, the large diameter afferents carrying touch **(L fiber)** and the small diameter afferents, e.g., Aδ and C fibers carrying pain **(S fiber)** both act upon an inhibitory neuron of substantia gelatinosa **(SG neuron)**.
      - ♦ Also, both of them stimulate the **T-cell** which is the pain afferent transmitted centrally from dorsal horn.
      - ♦ Now, activity in the large diameter afferent (L fiber) stimulates SG neuron which, in turn, inhibits stimulation of the T-cell by both L and S fibers. This explains inhibition of pain when large diameter afferents carrying touch sensation are stimulated. In this case, the gate is closed.
      - ♦ On the other hand, activity in the small diameter afferents inhibits SG neuron.
      - ♦ So, the inhibiting effect of SG neuron on T-cell stimulation by L and S fibers is removed. The gate is now open and activity in the small diameter pain fibers is transmitted centrally through T-cell.

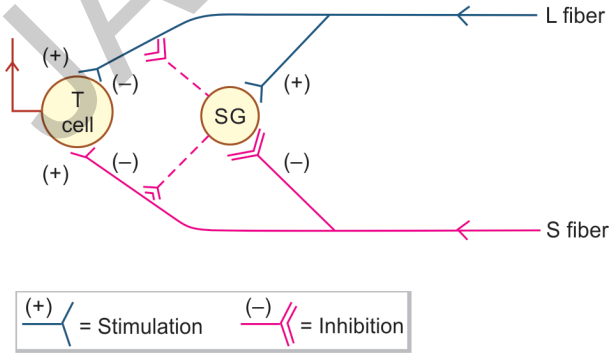


Fig. 81.9: Gate-control theory of pain. L fiber closes the gate while S fiber, by inhibiting SG neuron, opens the gate of pain transmission (see text).

   c. Electrical stimulation applied through electrodes in close proximity of the painful site relieves pain by stimulating large diameter nerve fibers. The mechanism is same as described above. This is called TENS (transcutaneous electrical nerve stimulation).
   d. Now it has been shown that the large diameter Aα or Aβ fibers carrying touch sensation causes secretion of GABA at the dorsal horn by interneurons. This GABA activates the $GABA_A$ and $GABA_B$ receptors located presynaptically on spinothalamic tract neurons. This blocks release of neurotransmitters from the spinothalamic tract afferents and thus prevents pain transmission during stimulation of touch fibers.
2. **Endogenous pain-inhibiting mechanism (Fig. 81.10)**
Opioid peptides (*see* p. 607) play a major role in this mechanism. Opioid peptides are pain-relieving endogenous neuropeptides/neuromodulators having actions like the opioid drug morphine. The endogenous opioid peptides may act at specific receptors at PAG, in the midbrain, at the dorsal horn or in the periphery.
   a. There are some specific areas in the midbrain which are concerned with pain inhibition. **PAG or periaqueductal gray present in the midbrain** is one

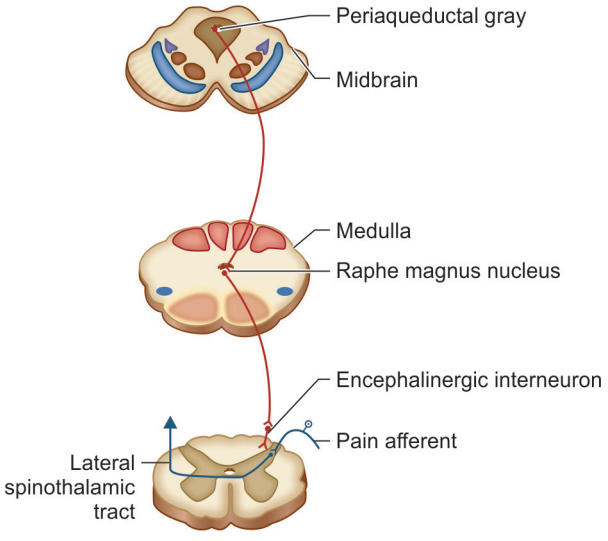


Fig. 81.10: Simplified diagram of endogenous pain-inhibiting mechanism (see text).

JAYPEE BROTHERS

such area playing an important role in endogenous pain inhibition.

b. PAG, on stimulation by opioid peptides, sends impulses through descending encephalinergic fiber to **Raphe magnus nucleus**, another important nucleus in the descending pain-inhibiting pathway.

c. Raphe magnus nucleus situated in the medulla, in turn, gives off descending serotonergic fiber which probably ends on **another encephalinergic interneuron**. The exact mechanism is not known but the following hypothesis may be put forward.

d. The encephalinergic interneuron is believed to terminate on the opioid receptors present on the **presynaptic sites** on the pain afferents of the dorsal horn and also on **postsynaptic sites** on the dendrites of spinothalamic tract neurons. The opioid peptide encephalin released from the encephalinergic interneuron, by acting on the presynaptic opioid receptors, inhibits release of glutamate and substance P, the neurotransmitters involved in impulse transmission through the pain-conducting lateral spinothalamic tract.

e. Stimulation of the opioid receptor at the postsynaptic site leads to opening of K^+ channels with K^+ efflux, causing hyperpolarization of the postsynaptic neuron.

Both these changes at the presynaptic and postsynaptic sites lead to a decrease in EPSP, resulting in inhibition of pain transmission.

Pain-inhibiting mechanisms in acupuncture act through gate-control mechanism when acting locally while their remote effects probably involve endogenous pain-inhibiting mechanism.

f. It is surprising that although the opioids are inhibitory neurotransmitters, they can stimulate descending pain-inhibiting pathways. The probable explanation is that the descending pain-inhibiting pathways are normally inhibited by neurons from medulla and midbrain. Opioids, by antagonizing this inhibition, actually stimulate the analgesia system (*see* p. 554).

g. In addition to the above pathway, two other descending pathways (not shown in the diagram) play an important role in pain inhibition. The first pathway descends from **PAG to rostral ventromedial medulla** from where descending catecholaminergic neurons end on dorsal horn neurons. The other pathway also involving catecholamines descends from **locus coeruleus to dorsal horn neurons**.

THALAMIC PAIN SYNDROME

1. It is a condition characterized by defective function of thalamus mainly due to damage of the posterior thalamic nuclei, caused by blockage of thalamogeniculate artery.
2. The damaged thalamic nuclei are posteroventral or ventrolateral. The signs of this syndrome depend on the affected nuclei.

a. When posteroventral nuclei are damaged, there is:
- Loss of sensation in the opposite half of the body.
- Loss of awareness of the opposite limbs (thalamic phantom limb) due to interference with proprioceptive input.
- Heightened pain sensations.

b. When ventrolateral nuclei are damaged:
- Cerebellar efferents are interrupted leading to loss of muscle tone, muscle weakness, ataxia, and intention tremor.
- Damage to neurons going to globus pallidus leads to features of choreoathetosis.
- There is flexion of wrist with hyperextension of fingers. This position of the hand is called "thalamic hand".

SURGICAL PROCEDURES FOR RELIEF OF PAIN

1. *Anterolateral cordotomy*: The lateral spinothalamic tract carrying pain sensation is surgically disrupted by an incision on the anterolateral aspect of the spinal cord.
2. *Posterior rhizotomy*: In this operation, the dorsal root is transected, thereby interrupting all pain carrying fibers of the corresponding segment.
3. *Prefrontal lobotomy*: Here, the prefrontal lobe is surgically disconnected from the rest of the brain. The patient feels the pain but the unpleasantness is no longer felt (*see* p. 611).

HYPERALGESIA AND ALLODYNIA

In zones of inflammation, various cytokines and growth factors are released. These inflammatory mediators heighten or exaggerate pain sensations by facilitating pain perception or transmission. In such inflammatory areas, stimuli normally capable of producing only mild pain can produce severe pain. This is known as **hyperalgesia**.

On the other hand, pain sensation produced in such inflammatory areas in response to previously innocuous (painless) stimuli such as touch, is called **allodynia**.

It is believed that some pain fibers are at first "silent" or insensitive to painful stimulation.

But, once they are sensitized by the products of inflammation, they become sensitive to pain thereafter. It is this activation of additional pain afferents by inflammatory mediators that is supposed to mediate allodynia and hyperalgesia.

Primary and Secondary Hyperalgesia

Hyperalgesia can be of two types:

1. **Primary hyperalgesia:** Here, the pain receptors have become hypersensitive with lowering of pain threshold. Chemical products released by inflammation like sunburn sensitize pain receptors and cause this type of hyperalgesia.

JAYPEE BROTHERS

2. **Secondary hyperalgesia:** It is pain felt in the undamaged zones surrounding the injured site.

   Both primary and secondary hyperalgesia appear to be due to the activity of neuroactive chemical mediators. Primary hyperalgesia is probably due to the activity of bradykinin, histamine, prostaglandin, serotonin, leukotrienes, etc., whereas substances P, CGRP, glutamate, etc., are the likely mediators in secondary hyperalgesia. Slow, aching, and prolonged nature of these types of pain are due to the presence of chemical agents lying in contact with the pain receptors for prolonged periods.

CHRONIC PAIN

Sensitization producing chronic pain occurs at two levels—peripheral and central.

1. Mechanism of **sensitization of peripheral nociceptors** is as follows:
   a. Tissue injury leads to accumulation of a mixture of chemical mediators like histamine (released from mast cells), acetylcholine, ATP and serotonin (released from damaged endothelium). This, in turn, leads to release of bradykinin and prostaglandin which are mainly responsible for pain sensitization at the level of nociceptors. Prostaglandin is synthesized from arachidonic acid by cyclooxygenase (COX2) enzymes. That is why NSAIDs which inhibit prostaglandin synthesis, have a role in pain relief.
   b. Tissue injury releases nerve growth factor (NGF), mediated by inflammatory cytokines IL-1 and TNF. NGF binds to TrkA receptors and causes retrograde transmission of pain-sensitizing signals. Anti-NGF antibody has been used successfully in animals to relieve hyperalgesia.

      BDNF, another neurotrophin, secreted centrally at the dorsal horn, causes sensitization of dorsal horn neurons. So, BDNF antagonists have a potential role for pain relief.
2. Mechanism of **central sensitization at the level of dorsal horn**:
   a. Repetitive noxious stimulation leads to activation of NMDA receptors of glutamate at dorsal horn synapses. This, in conjunction with substance P, ultimately produces a state of central sensitization known as "wind-up". This is manifested by gradually increasing excitability of dorsal horn neurons by a mechanism similar to long-term potentiation. Second messenger-mediated pathways and gene activation may also play a role. This heightens pain sensation and may lead to progression to chronic pain states.
   b. Injury to nerve, in particular, activates microglia leading to secretion of inflammatory cytokines which cause increased transcription of cyclooxygenase enzymes and synthesis of prostaglandins. These prostaglandins increase neuronal excitability at the dorsal horn, thus mediating pain sensitization both at the peripheral and central level.

   Incidentally, microglia contain P2X receptor. Inhibitors of these purinergic receptors appear to give relief in chronic pain. This further substantiates the role of microglia in the production of chronic pain.

   Other therapeutic options in chronic pain include administration of NMDA receptor antagonists, e.g., ketamine, amantadine, etc.

   Neuropathic pain is a type of chronic pain caused by damage to nerves. Damage to peripheral nerves can cause peripheral neuropathic pain such as causalgia and phantom limb pain. **Causalgia** is a type of treatment-resistant pain which is probably caused by upregulation of Na^+ channels in dorsal root ganglion cells.

   Sometimes, sprouting from postganglionic sympathetic neurons into dorsal root ganglion cells may explain a type of causalgia relieved by blocking of sympathetic nerves.

   (Dorsal horn sensitization is responsible for phantom limb pain which may appear to arise from the nonexistent amputated limb. So, operation under local anesthesia produced by **injecting anesthetic drugs locally at the spine** or site of amputation, has been shown to be more effective than general anesthesia in preventing postoperative phantom limb pain).

ITCH SENSATION

Itch sensation is characterized by a compulsive urge to scratch. It has the following features:

1. Latest research has identified specific spots called itch spots which when stimulated, give rise to itch sensation. These itch spots are usually found in the close vicinity of superficially located, rapidly adapting, and unmyelinated naked nerve endings.

   Itch-specific pathways formed by unmyelinated nerve fibers of small diameter have also been identified in spinothalamic tract.
2. Itch sensation is stimulated by chemical agents such as histamine, kinins, etc.
3. Several diseases such as chronic renal failure, liver disorders, and AIDS, are often associated with intractable itching.
4. Itch sensation is relieved by scratching. The mechanism is similar to "gate control" mechanism of pain inhibition. Scratching stimulates large diameter sensory fibers, which through recurrent collaterals, inhibits sensory fibers carrying itch sensation. Scratching protects the body from small crawling insects which activate itch sensation.

TICKLE SENSATION

1. Whereas itch sensation is irritating, tickle is pleasurable.
2. Tickle sensation, like itch, may be initiated by moving touch sensations.

JAYPEE BROTHERS

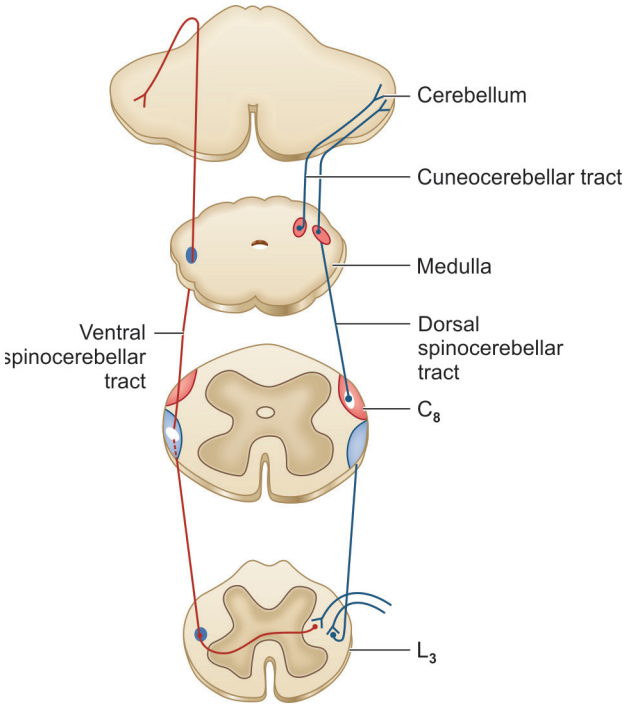


Fig. 81.11: Spinocerebellar tracts.

TEMPERATURE SENSATION

1. There are two types of temperature receptors. Both are free nerve endings. The cold receptors are stimulated by temperature between 10° and 38°C whereas the heat receptors are stimulated by temperature between 30°–45°C.
2. The cold receptors are innervated by both Aδ and C fibers whereas the heat receptors are innervated solely by C fibers.
3. The nerve pathways of temperature are similar to pain afferents, being carried by lateral spinothalamic tract, and ending in postcentral gyrus.
4. Good conductors of heat such as metallic objects stimulate temperature receptors more effectively as they alter the local temperature of these subcutaneous receptors more quickly. That is why a cool metallic object feels colder than a piece of wood of same temperature.

SPINOCEREBELLAR TRACTS (FIG. 81.11)

1. The spinocerebellar tracts mainly carry unconscious proprioceptive sensations from joints, muscles, and skin to the cerebellum.
2. These include the dorsal spinocerebellar tract and the ventral spinocerebellar tract which carry proprioceptive sensation from the inferior extremities and the lower part of the trunk.
3. Two other tracts, the cuneocerebellar tract and the rostral spinocerebellar tract carry proprioceptive sensations from the upper extremities and the upper part of the trunk.
4. The tracts:
   a. **The dorsal spinocerebellar tract:** Afferents from muscle spindle, joint receptors, Golgi tendon organs, etc., carrying proprioceptive input end in Clarke's column. Clarke's column is a nucleus located in lamina VII of the gray matter. Axons arising from this nucleus form the dorsal spinocerebellar tract. It passes ipsilaterally (on the same side) to the cerebellum through the inferior cerebellar peduncle.

      Some fibers of dorsal spinocerebellar tract carrying conscious proprioceptive sensation from ipsilateral lower limb end in nucleus Z, a group of neurons situated between upper end of nucleus gracilis and inferior vestibular nucleus.

      Fibers arising from nucleus Z join internal arcuate fibers and run along medial lemniscus to reach the thalamus on the way to cerebral cortex.
   b. **The ventral spinocerebellar tract:** Here also, the afferents carry sensation from peripheral proprioceptive receptors but mainly they transmit feedback from motor input to the anterior horn. The neurons mostly cross to the opposite side and move up through the medulla and pons to reach the midbrain.

      Ultimately, these fibers enter the same side of the cerebellum through the superior cerebellar peduncle by decussation in the cerebellar white matter. This is in keeping with the ipsilateral function of cerebellar cortex.
   c. **Cuneocerebellar tract:** In this tract, afferents carrying proprioceptive input from the upper extremity end in the lateral cuneate nucleus. From there, neurons pass through the inferior cerebellar peduncle and terminate in the cerebellum.
   d. **Rostral spinocerebellar tract:** It is organized in the same way as the ventral spinocerebellar tract.

      The main difference is that the rostral spinocerebellar tract carries information from the upper portions of the trunk and upper extremity whereas the ventral spinocerebellar tract carries information from the lower trunk and lower extremity.

      Also, its fibers enter the cerebellum through the inferior cerebellar peduncle unlike the ventral spinocerebellar tract which enters cerebellum through the superior cerebellar peduncle.

JAYPEE BROTHERS

for detailed information on physiology books, visit our website www.ejaypee.com, for detailed information on physiology books, visit our website www.ejaypee.com, for detailed information

Principles of Physiology

Salient Features

- It includes a concise coverage of physiological principles and competencies enumerated in CBME curriculum.
- New formatting style for easier memorization of keywords has been used.
- New tables and summaries have been added for easy retention of complex topics.
- A few important chapters have been rewritten entirely with improved presentation.
- A list of wide-ranging MCQs have been retained with helpful explanations while a list of probable questions including short notes have been added as per NMC guidelines.
- The usual student-friendly approach and lucid language have been maintained.

Debasis Pramanik MD (Cal) is presently working as Professor and Head, Department of Physiology, KPC Medical College and Hospital, Kolkata, West Bengal, India. He is a sincere and devoted "lifelong learner" of Physiology, the mother subject of Medical Sciences.

He is one of the seniormost teachers in Physiology in the state with more than 36 years of teaching experience.

diginerve® A Jaypee Initiative
• Video Lectures • Dr. Wise AI Chatbot
• Question Bank • Notes
Download App

Buy from ejaypee
JAYPEE BROTHERS

Shelving Recommendation
PHYSIOLOGY

ISBN 978-93-6616-299-7
9 789366 162997