

Pu Cı



Textbook of Pulmonary & Critical Care Medicine

Forewords
JS Guleria
Atul C Mehta

Editor-in-Chief
Surinder K Jindal

Forewords
JS Guleria
Atul C Mehta

3_{rd}



Contents

Volume 1

	SECTION 1: HISTORY AND DEVELOPMENT	
1.	History of Respiratory Medicine Surinder K Jindal Ancient History 3; Modern, Postbiblical Period 5; Contemporary Respiratory Medicine 7	3
2.	Anatomy and Architecture: A Clinical Perspective Surinder K Jindal Lung Anatomy and Morphology 9; Architecture of Lung Parenchyma 12; Blood Supply of Lungs 13; Lymphatic Drainage 14; Nerve Supply 14; Thoracic Cage 15	9
3.	Lung Development Meenu Singh, Nidhi Anil, Amit Agarwal Development of Airway Epithelium 17; Pulmonary Vasculature 18; Beginning of Postnatal Life 19; Role of Stem Cells in Lung Development 20	17
	SECTION 2: RESPIRATORY PHYSIOLOGY	
4.	Applied Respiratory Physics VK Jindal, Surinder K Jindal State of Matter 25; Physical Properties of Gases 26; Gas Laws 28; Gas Solution and Tension 29; Vapors 29; Expression of Gas Volumes and Pressures 30; Flow of Gases 30	25
	Applied Respiratory Physics VK Jindal, Surinder K Jindal State of Matter 25; Physical Properties of Gases 26; Gas Laws 28; Gas Solution and Tension 29;	25 34

7.	Oxygen Transport and Tissue Oxygenation Surinder K Jindal	62
	Oxygen Transport 62; Oxygen Delivery 62; Oxygen Consumption 64; Oxygen Extraction Ratio 65; Oxygen Delivery–Oxygen Consumption Curve 65; Assessment of Tissue Oxygenation 66	
8.	Respiratory Function in Specific Physiological States Sunil K Chhabra, Mansi Gupta	68
	Exercise 68; Pregnancy 71; High Altitude 73; Deep Diving 75	
9.	Respiratory Muscle Function	80
	Randeep Guleria	
	Respiratory Muscles—Anatomical Consideration 80; Respiratory Muscles: Basic physiology 81; Evaluation of Respiratory Muscle Function 82; Function Testing 83; Electrophysiological Assessment of Respiratory Muscles 87; Respiratory Muscle Endurance 88	
10.	The Aging Lung	92
	Richard Henriquez, Daniel E Banks	
	Physiology: A Starting Point 93; Cells and Structural Features of the Aging Lung 95; Selected Lung Diseases and Aging 99	
11.	Respiratory Defenses and Immunology	106
	Padmavathi Ramaswamy, Padma Srikanth, Vijayalakshmi Thanasekaraan	
	Particle Deposition in the Respiratory Tract 106; Defense Mechanisms of Conducting Zone of the Airways 107; Defense Mechanisms of Respiratory Zone of the Airways 110; Surfactant and Surfactant Protein A 112; Respiratory Immune Mechanisms 112; Innate Immunity and Toll-like Receptors 112; Alveolar Macrophages 112; Adaptive Immunity 113; Role of Immunoglobulins 114; Impact of Bacteria and Viruses on Lung Immunology 115; Human Leukocyte Antigen and Mycobacterial Diseases 116; Mucosal Vaccines for Respiratory Infections 116; Lung Microbiome 116	
	SECTION 3: RISK FACTORS FOR RESPIRATORY DISEASES	
12.	Genomics of Lung Diseases	121
	Mayank Garg, Anurag Agrawal	
	Approach to Genetic Studies 122; Genomics of Lung Disorders 122; Pharmacogenomics in Lung Disorders 126; Future Directions 126	
13.	Aging, Chronic Lung Disease and the Emerging Horizon	
	of Regenerative Medicine	129
	Sudheendra Ghosh C, Sarun Ghosh	
	Definition of Aging 129; Chronic Obstructive Pulmonary Disease and Growing Older 131; Regenerative Medicine 133	
14.	Sex and Gender Perspectives of Pulmonary Disorders	135
	Kumari Indira KS, Vijayalakshmi Thanasekaraan	
	Sex and Gender 135; Sex Dimorphism in Structure and Functions 135; Sex-specific Gene Mutations 135	

15.	Body Weight as a Risk Factor for Lung Diseases	143
	Basanta Hazarika, Farjana Begum	
	Physiological Changes 143; Obesity and Chronic Obstructive Pulmonary Disease 144; Obesity and Asthma 145; Obesity and Obstructive Sleep Apnea 145; Obesity and Obesity–Hypoventilation Syndrome 146; Obesity and Pneumonia 146; Obesity and Deep Venous Thrombosis/Pulmonary Embolism 146; Obesity and Pulmonary Hypertension 147; Obesity and Lung Fibrosis 147; Weight Reduction 147	
16.	Tobacco Smoking	150
	Virendra Singh, Bharat Bhushan Sharma	
	Tobacco Smoking 150; Smoking-control Interventions 153	
17.	Outdoor Air Pollution and Respiratory Health	161
	Sara Maio, Sandra Baldacci, Giuseppe Sarno, Sofia Tagliaferro, Ilaria Stanisci, Stefania La Grutta, Giovanni Viegi	
	Outdoor Air Pollution Effects 161	
18.	Risk Factors for Respiratory Diseases: Indoor Air Pollution	170
	Giuseppe Sarno, Sara Maio, Sandra Baldacci, Ilaria Stanisci,Sofia Tagliaferro, Stefania La Grutta, Giovanni Viegi	
	Indoor Pollutants and Related Sources 171	
	CECTION A DECDIDATION OF DIAGNOSIS	
	SECTION 4: RESPIRATORY DIAGNOSIS	
art A	SECTION 4: RESPIRATORY DIAGNOSIS	
	: Clinical Approach	181
		181
	: Clinical Approach Cough in the Adult	181
19.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183	181
	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183	
19.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis	
19. 20.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis Catherine M Fiore, J Mark Madison, Rahul N Sood Anatomy 195; Etiology and Pathogenesis 195; Treatment 202	195
19.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis Catherine M Fiore, J Mark Madison, Rahul N Sood Anatomy 195; Etiology and Pathogenesis 195; Treatment 202 Dyspnea	
19. 20.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis Catherine M Fiore, J Mark Madison, Rahul N Sood Anatomy 195; Etiology and Pathogenesis 195; Treatment 202	195
19. 20. 21.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis Catherine M Fiore, J Mark Madison, Rahul N Sood Anatomy 195; Etiology and Pathogenesis 195; Treatment 202 Dyspnea Allyson Hughes, Anna Rudnicki, J Mark Madison Physiology 207; Positional and Nocturnal Dyspnea 209; Evaluating Acute Dyspnea 209;	195
19. 20. 21.	Cough in the Adult Evan W Jones, Edward W Adams, Scott E Kopec Epidemiology 181; Physiology 181; Pathophysiology 181; Benefits of Cough 182; Complications of Cough 182; Causes of Cough 183 Hemoptysis Catherine M Fiore, J Mark Madison, Rahul N Sood Anatomy 195; Etiology and Pathogenesis 195; Treatment 202 Dyspnea Allyson Hughes, Anna Rudnicki, J Mark Madison Physiology 207; Positional and Nocturnal Dyspnea 209; Evaluating Acute Dyspnea 209; Evaluating Chronic Dyspnea 209; Treatment 210	195 207

23.	History and Physical Examination	221
	PR Gupta	
	History Taking 221; History of Treatment 223; Physical Examination 223	
24.	Biomarkers in Lung Diseases	230
	Nikhil C Sarangdhar	
	Applications, Roles, and Prospects of Biomarkers in Pulmonary Diseases 230; Biomarkers in Pulmonary Diseases—Current Status 231	
art B	: Chest Imaging	
25.	Systematic Approach to Interpretation of Plain Chest Radiographs D Behera	242
	Posteroanterior View 242; Anteroposterior View 242; Lateral View 242; Apicogram 242; Oblique View 242; Lateral Decubitus Films 243; Expiratory Skiagrams 243; Fluoroscopy 243; Reading a Chest X-ray 243; Abnormal Radiological Findings 246; Airspace Disease 249; Parenchymal Atelectasis 252; Metastasis 252; Fibrosis 253; Interstitial Disease 253; Silhouette Sign 260; Mediastinal and Hilar Shadows 261	
26.	Role of CT Scan for Lung Lesions: A Systematic Approach	267
	Richa Gupta, Prince James	
	Indications for CT Thorax 267; Types of CT Scan/CT Scan Protocol 267; Systemic Approach to Read CT 268; Systemic Interpretation 269; Additional Findings 275; Technical Pitfalls 275	
27.	Systematic Approach to Diagnosing Diffuse Lung Disease on	
	High-resolution CT Scans	278
	Jacob Schwartz, James Gruden, Stephen Machnicki, Kevin Shayani, Suhail Raoof	
	Lung Anatomy 278	
28.	Novel Imaging to Assess Airway Diseases	291
	Carmen Venegas Garrido, Sarah Svenningsen, Parameswaran Nair	
	Novel Imaging Modalities and Their Role in Airway Diseases 291; What can be Measured by Novel Pulmonary Imaging? 291; Description and Applicability of Different Novel Imaging Techniques 292; Clinical Applications 293; Limitations 295	
29.	Nuclear Imaging in Pulmonary Medicine	298
	BR Mittal, Kanhaiyalal Agrawal	
	Pulmonary Anatomy and Physiology 298; Investigations 299; Interpretation Criteria 302	
30.	Thoracic Ultrasound	311
	Mahismita Patro, Anshul Jain, Dipti Gothi	
	Principle of Ultrasound 311; Technical Characteristics 311; Patient and Probe Positioning 312; Normal Thoracic Ultrasound Findings 312; Thoracic Ultrasound in Pathology 313; Ultrasound-guided Interventions 317; Role of Ultrasound in Critical Care 318	

Part C	: Lung Function Tests	
31.	Pulmonary Function Tests: Part I Ashutosh Nath Aggarwal	322
	Spirometry 323; Peak Expiratory Flow 327; Static Lung Volumes 328; Diffusing Capacity of Lungs 330; Exercise Testing 331; Other Tests 333	
32.	Pulmonary Function Tests: Part II	337
	Deepak Talwar, Kanishka Kumar, Dhruv Talwar	
	Lung Oscillometry 337; Lung Clearance Index 338; Breath Tests (Breathomics) 341; Fractional Exhaled Breath Nitric Oxide 342; 6-Minute Walk Test 344	
33.	Arterial Blood Gas Monitoring	348
	Vikram Damaraju, Inderpaul Singh Sehgal, Ritesh Agarwal	
	Arterial Sampling 348; Continuous Intra-arterial Blood Gas Monitoring 350; Noninvasive Blood Gas Monitoring 350	
34.	Interpretation of Acid-Base Balance	357
	Aditya Jindal	
	Basic Concepts 357; Acid Regulation 358; Types of Acid–base Disorders 358; Acid–base Disorders 361; Arterial versus Venous Blood for Blood Gas Analysis 364	
Part D	: Thoracic Endoscopy	
35.	Panorama of Bronchoscopy: Fundamentals, Diagnostics, and Interventions	367
	Sameer Bansal, Kaumudi Devi, Ravindra Mehta	
	Tracing the Evolution of Bronchoscopy and Interventional Pulmonology 367; Sedation for Bronchoscopy 369; Accessories for Bronchoscopy 369; Diagnostic Bronchoscopy 376; Therapeutic Bronchoscopy 379; Latest Advancements 383	
36.	Medical Thoracoscopy	387
	Ravindran C, Jyothi E	
	Medical Thoracoscopy 387	
	SECTION 5: TUBERCULOSIS	
37.	Epidemiology and Burden of Tuberculosis Sanjeev Nair	399

Global Burden of Tuberculosis 399; Burden of Tuberculosis in India 400;

Evolving Strategies for Tuberculosis Control/Elimination in the World and India 402; Tuberculosis Infection and Disease 403; Burden of Drug-resistant TB and HIV-TB 405; Different Forms of Tuberculosis 406; Global Progress toward Achieving End-TB Targets 406

38.	Risk Factors for Tuberculosis	408
	Nargis K Bali, Parvaiz A Koul, Hazique Parvaiz Koul	
	Medical Illnesses 408; Sociodemographic Factors 411; Others Risk Factors 412	
39.	Mycobacteria: An Overview	415
	Kritika Kakkar, Romica Latawa, Stuti Aggarwal, Indu Verma	
	Route and Spread of Infection 415; Spectrum of Tuberculosis Disease 415; Mycobacterial Groups 416; Emerging Mycobacterial Species 416; Cell Wall Structure 417; Mycobacterial Genome 417; Mycobacterial Identification 417; Mycobacterial Drug Resistance 418	
40.	Tuberculosis Immunology and Pathogenesis	421
	Ankit Kumar, Madhur Kalyan, Krishna K Singh, Indu Verma	
	<i>Mycobacterium tuberculosis</i> Infection and Overview of Immunopathogenesis 421; Immune Responses to Tuberculosis 422; Immune Responses in Tuberculosis with Comorbid Condition 427	
41.	Pulmonary Tuberculosis: Clinical Features and Diagnosis	431
	Surender Kashyap, Malay Sarkar	
	Postprimary Pulmonary Tuberculosis 431; Symptoms and Signs 431; Tuberculosis in the Elderly 433; Miliary Tuberculosis 433; HIV and Tuberculosis 433; Pleural Effusion 433; Paradoxical Response 434; Subclinical and Incipient Tuberculosis 434; Physical Examination 434; Diagnosis of Tuberculosis 434; Extrapulmonary Tuberculosis 440	
42.	Molecular Diagnosis of Tuberculosis	443
	Anjali Kashwal, Sumedha Sharma, Ramamurthy Sakamuri, Mamta Kalra, Suman Laal, Indu Verma	
	Diagnosis of Tuberculosis: Active Infection 443; Diagnosis of Tuberculosis: Latent Infection 444; Tuberculosis Diagnosis in Human Immunodeficiency Virus-positive Individuals 444; Diagnosis of Tuberculosis: Beyond Microscopy 444	
43.	Management of Tuberculosis	452
	D Behera	
	Chemotherapy of Tuberculosis 452; Supervision of Chemotherapy 456; Extrapulmonary Tuberculosis 458; Drug-resistant Tuberculosis 458	
44.	Antitubercular Drugs	466
	Subodh Kumar Katiyar, Sandeep Katiyar	
	Isoniazid 467; Rifampicin 468; Streptomycin 470; Pyrazinamide 470; Ethambutol 471; Quinolones–Fluoroquinolones 471; Ethionamide/Prothionamide 473; Cycloserine/Terizidone 473; Aminoglycosides and Capreomycin 474; Beta-lactam—Amoxicillin/Clavulanate 474; Macrolides: Clarithromycin and Azithromycin 475; Thioacetazone 475; Newer Drugs 475; Repurposed Drugs 478; Restored Drugs 480; Optimized Drugs 481; Underutilized Drugs 482	
45.	Latent Tuberculosis and Prevention	488
	Rohit Sareen, Vikram Vohra, JK Saini	
	Latent Tuberculosis and Tuberculosis Preventive Treatment 488; Tuberculosis Vaccines 492; Infection Prevention and Control 493	

46.	Extrapulmonary Tuberculosis	499
	Ashok K Janmeja, Prasanta Raghab Mohapatra, Deepak Aggarwal	
	Diagnosis 499; Lymph Node Tuberculosis 500; Pleural Effusion 501; Bone and Joint Tuberculosis 503; Central Nervous System Tuberculosis 504; Abdominal Tuberculosis 506; Genitourinary Tuberculosis 508; Skin Tuberculosis 509; Miliary Tuberculosis 510; Pericardial Tuberculosis 512; Hepatic Tuberculosis 513	
47.	Post-tuberculosis Pulmonary Sequelae	516
	Surya Kant, Ankit Kumar	
	Pathogenesis of Post-tuberculosis Pulmonary Sequelae 519; Clinical Presentation and Diagnosis 519; Diagnostic Methods 519; Management 520; Prevention and Public Health Implications 520	
48.	Multidrug-resistant Tuberculosis	521
	SK Sharma, Alladi Mohan	
	Definitions 521; Basis of Drug Resistance 521; Epidemiology 521; Diagnosis 523; Management 524; Multidrug-resistant Tuberculosis in Special Conditions 530	
49.	Treatment of Tuberculosis in Special Situations	534
	Rajendra Prasad, Nikhil Gupta, Rishabh Kacker	
	Pharmacokinetics of Antitubercular Drugs 534; Treatment of Tuberculosis in Pregnancy and Lactation 535; Treatment of Tuberculosis in Renal Insufficiency 536; Treatment of Tuberculosis in Liver Disease 537; Drug-induced Hepatotoxicity 537; Antituberculosis Treatment with Pre-existing Liver Disease 538; Antituberculosis Treatment In Patients with QT Prolongation 539	
50.	Tuberculosis and Human Immunodeficiency Virus Infection	541
	Aditya Jindal	
	Epidemiology 541; Pathogenesis 542; Clinical Features 543; Diagnosis 544; Management 544	
51.	Nontuberculous Mycobacterial Disease	549
	Anant Mohan, Irfan Shekh, Rohit Vadala	
	Epidemiology of Nontuberculous Mycobacterial Infections 549; Clinical Spectrum of Nontuberculous Mycobacteria Infections 551; Diagnosis of Nontuberculous Mycobacteria Pulmonary Infections 553; Treatment of Pulmonary Nontuberculous Mycobacteria Infection 553; Definitions of Microbiological Outcome 556	
	SECTION 6: NONTUBERCULAR RESPIRATORY INFECTION	
52.	Microbiological Approach to Respiratory Infections	561
	Pallab Ray	
	Upper Respiratory Tract Infections 561; Lower Respiratory Tract Infections 565	
53.	Community-acquired Pneumonia	571
	Ashish Kumar Prakash, Bornali Datta	
	Definitions 571; Classification of Pneumonia 571; Etiopathogenesis 571; Clinical Evaluation 573; Diagnostic Approach 574; Treatment of Pneumonia 574	

54.	Nosocomial Pneumonia Vishwanath Gella, Sivakumar L	577
	Definitions 577; Pathogenesis 577; Prevention 578; Diagnosis 581; Treatment 584	
55.	Pneumonia in Immunocompromised Hosts Mansi Gupta, Riksoam Chatterjee Epidemiology 590; Pathophysiology 591; Etiology 593; Diagnosis 595; Management 603	590
56.	Pulmonary Fungal Infections Arunaloke Chakrabarti Epidemiology 607; Types of Fungi 608; Pneumocystis Respiratory Tract Infection 613	607
57.	Pulmonary Mycetoma Alladi Mohan, Abha Chandra, B Vijayalakshmi Devi Pathogenesis 621; Pathology 622; Clinical Presentation 622; Diagnosis 624; Treatment 626; Prognostic Factors 629; Overall Mortality 629	621
58.	Viral Pneumonias Arjun Srinivasan, Ritesh Agarwal Respiratory Viruses 632; Presenting Features 633; Rapid Diagnostic Modalities for Respiratory Viruses 633; Varicella Pneumonia 633; Cytomegalovirus Pneumonia 634; Coronavirus-associated Respiratory Illnesses 635; Adenovirus Pneumonia 638; Influenza 638; Risk Factors and Features of Severe Disease 640; Respiratory Protection for Healthcare Professionals 640; Diagnosis 641; Antiviral Therapy 641; Management of Critically Ill Patients with H1N1 Influenza 2009 641; H1N1 Influenza 2009 Monovalent Vaccine 642	632
59.	COVID-19 Pandemic: A Summary Review Surinder K Jindal Picture 644; Diagnosis 645; Complications 646; Management at Different Levels of Care 647;	644
	Preventing the Spread: Public Health Interventions 650	
60.	COVID-19 Management Javid Ahmad Malik, Aqeel Hussain Antiviral Agents 653; Immunomodulators 654; Anticoagulant and Antithrombotic Therapy 656; Management of COVID-19 Acute Respiratory Distress Syndrome 656; Vaccination 656	653
	COVID-19 Management Javid Ahmad Malik, Aqeel Hussain Antiviral Agents 653; Immunomodulators 654; Anticoagulant and Antithrombotic Therapy 656;	653 659
61.	COVID-19 Management Javid Ahmad Malik, Aqeel Hussain Antiviral Agents 653; Immunomodulators 654; Anticoagulant and Antithrombotic Therapy 656; Management of COVID-19 Acute Respiratory Distress Syndrome 656; Vaccination 656 Post-COVID Lung Sequelae Bharat Gopal Post-COVID Disease-Delphi Consensus 659; Post-COVID Sequelae: Epidemiology 659; Physiology of Post-COVID Sequelae 660;	

64.	Bronchiectasis	681
	Raja Dhar, Shubham Sharma	
	Types 681; Epidemiology 681; Pathophysiology 681; Etiology 682; Diagnostic Evaluation 684; Treatment Strategies 684; Prognosis and Follow-up 685; Patient Education and Self-management 685	
65.	Rare Respiratory Infections	688
	Mohankumar Thekkinkattil	
	Viral Infections 688; Rare Forms of Tuberculous Infections 689; Atypical Bacterial Infections 689; Parasitic Infections 691	
66.	Parasitic Diseases of Lung	694
	Udas Chandra Ghosh, Avisek Gon, Abhinaba Datta	
	Clinical Syndromes 694; Löffler Syndrome 694; Pulmonary Filariasis (Tropical Pulmonary Eosinophilia) 696; Visceral Larva Migrans 697; Hydatid Disease 697; Schistosomiasis 699; Paragonimiasis 699	
67.	Anaerobic Bacterial Infections of the Lungs and the Pleura	702
	Ashok Shah, Chandramani Panjabi	
	Pathophysiology 702; Natural History and Clinical Classification 703; Anaerobes and Upper Respiratory Syndromes 704; Microbiology 705; Clinical Features 706; Laboratory Diagnosis 707; Radiological Manifestations 709; Treatment 709; Prognosis 710; COVID-19 and Anaerobic Respiratory Infections 710	
68.	Pulmonary Involvement in Common Tropical Diseases	713
	Surinder K Jindal, Sanjay Jain	
	Malaria 713; Typhoid 715; Leptospirosis 716; Dengue 716; Amebiasis 717	
69.	Respiratory Infections in Children	720
	Sambita Panda, Sarvendra Vikram Singh, Aravindan Karthikeyan	
	Upper Respiratory Tract Infections 720; Lower Respiratory Tract Infections 721; Pulmonary Manifestations of HIV Infection in Children 722; Tuberculosis and Multidrug-resistant Tuberculosis in Children 723	
70.	Antimicrobial Agents: Antibacterial and Antiviral Drugs	726
,	Mahesh Kumar Balasundaram, Nusrat Shafiq, Samir Malhotra	, =0
	Beta-lactams 726; Antiviral Drugs 741	
71	Antifum not Amonto	746
/1.	Antifungal Agents	746
	J Whig, Bharti Mahajan, Rajesh Mahajan Polyanas, 746, Azalas, 747, Antimatahalitas (Nyalassida Analass, 740, Specific Issues, 751)	
	Polyenes 746; Azoles 747; Antimetabolites/Nucleoside Analogs 749; Specific Issues 751	
	SECTION 7: BRONCHIAL ASTHMA	
72.	. 37	757
	Pawan Tiwari, Lt Col (Dr) Rahul Tyagi Definition, 757: Enidemiology, 757: Disk Easters for Arthma, 759: Natural History, 750	
	Definition 757; Epidemiology 757; Risk Factors for Asthma 758; Natural History 759	

73.	Airway Inflammation and Remodeling in Asthma SN Gaur, Nikhil C Sarangdhar	761
	Airway Inflammation 761; Asthma Phenotypes 761; Airway Remodeling 766; Asthma: An Epithelial Disease 766; Tests to Detect Airway Remodeling 768; Effects of Drugs and Other Therapeutic Interventions on Airway Remodeling 769; Prevention of Airway Remodeling 769	
74.	Bronchial Asthma: Diagnosis	772
	Vishal Chopra, Rahul Suri, Siddharth Chopra	
	Clinical Diagnosis 772; Medical History 772; Physical Examination 773; Objective Measurements of Lung Function 774; Evaluation of Asthma 776; Diagnostic Challenges 777	
75.	Asthma Triggers and Risk Factors	780
	SK Gupta, Puja Garg	
	What is a Trigger? 780; Asthma Trigger Avoidance and Control of Asthma 782	
76.	Asthma Comorbidities	786
	Parthasarathi Bhattacharyya	
	Gastroesophageal Reflux Disease 786; Allergic Rhinitis and Nonallergic Rhinitis 787; Psychological Disturbance and Asthma 788; Obesity 788; Obstructive Sleep Apnea 788; Respiratory Infections 788; Dysfunctional Breathing and Vocal Cord Dysfunction Syndrome 789; Chronic Obstructive Pulmonary Disease 789; Osteoporosis 789; Management of Asthma Comorbidities 789	
77.	Control and Management of Stable Asthma	792
	Sidney S Braman, Katherine E Hodgin	
	Goals of Asthma Treatment 792; Essential Components of Asthma Care 793; Treatment of Stable Asthma 798; Treatment Protocols for Asthma 804; Asthma Control in Developing Countries 806	
78.	Acute Asthma Exacerbations	812
	Aditya Jindal	
	Triggers Causing Exacerbations 812; Diagnosis and Evaluation of Severity 813; Management 813	
79.	Severe Asthma: Phenotypes and Management	819
	Uma Devaraj, Uma Maheswari Krishnaswamy	
	Definition of Severe Asthma 819; Genetics of Severe Asthma 820; Asthma Phenotypes and Endotypes 820; Rationale for Characterizing Severe Asthma Phenotypes 822; Diagnosis of Severe Asthma 824; Treatment of Severe Asthma 824	
80.	Allergen Desensitization	828
	Vikram Jaggi	
	Definition 828; Historical Background 828; Mechanisms of Allergen Immunotherapy 829; Future Directions 833	
81.	Nonpharmacological Management	835
	Surya Kant, Anuj Kumar Pandey	
	Nonpharmacological Modalities for Managing Bronchial Asthma 835	

82. Allergic Bronchopulmonary Aspergillosis

840

Ritesh Agarwal, Valliappan Muthu, Inderpaul Singh Sehgal

Characterization of *Aspergillus* Species 840; Epidemiology of Allergic Bronchopulmonary Aspergillosis 841; Pathogenesis of Allergic Bronchopulmonary Aspergillosis 841; Pathology of Allergic Bronchopulmonary Aspergillosis 843; Clinical Features 843; Laboratory Findings 844; Diagnostic Criteria 848; Natural History 848; Management 852; Treatment Protocol 855; Differential Diagnosis 856; Complications 856; Allergic Bronchopulmonary Aspergillosis Sans Asthma 856; Allergic Bronchopulmonary Aspergillosis in Cystic Fibrosis 857; Coexistence of Allergic Bronchopulmonary Aspergillosis and Aspergilloma 857; Allergic Bronchopulmonary Mycosis 857; Allergic Bronchopulmonary Aspergillosis Complicating Other Conditions 857; Sinobronchial Allergic Mycosis Syndrome 858

Volume 2

SECTION 8: OBSTRUCTIVE PULMONARY DISEASES

83. Chronic Obstructive Pulmonary Disease: Epidemiology, Burden, and Risk Factors Surinder K Jindal

Epidemiology 873; Risk Factors 875

84. An Appraisal of Chronic Obstructive Pulmonary Disease in Low- and Middle-income Countries

881

873

Mohammad Azizur Rahman, Pajanivel Ranganadin, Varuna Jethani

Epidemiology 881; Risk Factors of Chronic Obstructive Pulmonary Disease 881; Salient Clinical Features 883; Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease in Low- and Middle-income Countries 883

85. Chronic Obstructive Pulmonary Disease: Pathogenesis, Clinical Features and Diagnosis

885

Aditya Jindal

Pathogenesis and Pathophysiology 885; Clinical Features 887; Diagnosis of Chronic Obstructive Pulmonary Disease 888

86. Systemic Manifestations and Comorbidities of Chronic Obstructive Pulmonary Disease

891

Agam Vora

Chronic Obstructive Pulmonary Disease and Cardiovascular Disease 891; Systemic Venous Thromboembolism and Chronic Obstructive Pulmonary Disease 891; Pulmonary Hypertension and Chronic Obstructive Pulmonary Disease 892; Pulmonary Embolism 892; Pneumonia 893; Lung Cancer 893; Musculoskeletal Dysfunction 893; Malnutrition in Chronic Obstructive Pulmonary Disease Patients 893; Osteoporosis In Chronic Obstructive Pulmonary Disease Patients 893; Gastroesophageal Reflux 894; Diabetes Mellitus 894; Anxiety and Depression Disorders 894; Sleep Disturbance 894

87.	Treatment of Chronic Obstructive Pulmonary Disease Peter J Barnes	897
	Prevention and Risk Factors 897; Bronchodilators 899; Corticosteroids 903; Phosphodiesterase Inhibitors 904; Supplementary Oxygen 904; Antibiotics 905; Other Drug Therapies 905; Nonpharmacological Treatments 906; Managing Chronic Disease 907; Treatment of Acute Exacerbations 908; Treatment of Cor Pulmonale 908; Future Therapies 908	
88.	Exacerbations of Chronic Obstructive Pulmonary Disease	912
	Raja Dhar, Aloke Gopal Ghoshal, Tarang Kulkarni	
	Definition and Severity of Chronic Obstructive Pulmonary Disease Exacerbation 912; Pathophysiology of Exacerbation of Chronic Obstructive Pulmonary Disease 913; Symptoms of Exacerbation of Chronic Obstructive Pulmonary Disease 914; Management of Exacerbation of Chronic Obstructive Pulmonary Disease 914; Prognostication of Chronic Obstructive Pulmonary Disease Exacerbations 915; Outpatient Management for Exacerbation of Chronic Obstructive Pulmonary Disease 916; Inpatient Management of Exacerbation of Chronic Obstructive Pulmonary Disease 916; Pharmacological Management 916; Discharge Planning 919; Prevention of Exacerbation of Chronic Obstructive Pulmonary Disease 919	
89.	Palliative Care and End-of-life Communication in Advanced	
	Chronic Obstructive Pulmonary Disease	923
	Sujeet Rajan, Rohit Joshi	
	Definitions 923; Palliative Care Before End-of-life 923; Advanced Terminal Chronic Obstructive Pulmonary Disease 924; Good Death in Chronic Obstructive Pulmonary Disease: Implications 925; Appropriate Time to Begin Discussions on End-of-life Issues with Chronic Obstructive Pulmonary Disease Patients 925; Principles of End-of-Life Communication in Chronic Obstructive Pulmonary Disease 926	
90.	Pulmonary Rehabilitation	929
	Deepak Talwar, Mir Shad Ali, Dhruv Talwar	
	Disability Associated with Chronic Obstructive Pulmonary Disease 929; Systemic Consequences of Chronic Obstructive Pulmonary Disease 930; Role of Pulmonary Rehabilitation 930; Definition and Goals of Pulmonary Rehabilitation 931; Indications for Pulmonary Rehabilitation—Who to Refer? 931; Assessment for Pulmonary Rehabilitation Program 931; Common Outcome Measures 932; Core Components of a Pulmonary Rehabilitation Program 933; Duration and Frequency of a Pulmonary Rehabilitation Program 935; Long Term/Maintenance 935; Oxygen 935; Mobility Aids 935; Pulmonary Rehabilitation Team 936; Quality Assurance and Audit 936; Location and Settings of Pulmonary Rehabilitation 936; Exacerbations 936; Training Adjuncts or Strategies 936; Home-based Pulmonary Rehabilitation 936; Virtual Pulmonary Rehabilitation 937	
91.	Bullous Lung Diseases	940
	Aditya Jindal, Gyanendra Agrawal	
	Pathogenesis 940; Etiology 941; Clinical Presentation 941; Radiologic Features 941; Pulmonary Function Tests 942; Natural History 943; Complications 943; Treatment 943	
92.	Upper and Central Airway Obstruction	946
	VR Pattabhi Raman, Arun Raja	
	Types of Upper Airways Obstruction 946; Anatomic Differences of the Airway in Infants/Children and its Consequences 946; Clinical Features 947; Diagnosis 947; Acute Upper Airway Obstruction 949; Chronic Upper Airway Obstruction 949; Therapeutic Considerations 956	
93.	Chronic Respiratory Failure	959
	Jennifer Trevor, Lanier O'Hare	
	Chronic Hypoxemic Respiratory Failure 959; Chronic Hypercapnic Respiratory Failure 961; Management of Chronic Respiratory Failure 961	

SECTION 9: ENVIRONMENTAL AND OCCUPATIONAL DISORDERS 94. Lung Disease in Coal Workers 967 Harakh V Dedhia, Daniel E Banks Epidemiologic Features of Coal-induced Lung Disease 968; Clinical Features of Coal Dust Exposure 969; Pathology of Coal Workers' Pneumoconiosis 972; Management of Coal Mine Dust-induced Lung Disease 975 95. Silicosis 980 Surinder K Jindal, PS Shankar Silica and Silicosis 980; Problem of Silicosis in India 980; Problem of Silicosis in Other Asian Countries 981; Pathogenesis 981; Types of Silicosis 981; Clinical Features 982; Diagnosis 982; Radiographic Patterns 983; Pulmonary Functions 983; Other Investigations 983; Complications 984; Prognosis 985; Treatment 985; Prevention 985 96. Metal-induced Lung Diseases 988 Nikhil C Sarangdhar, Dilip V Maydeo Clinical Classification of Metal-induced Lung Diseases 988; Epidemiology and Risk Factors 988; Pathogenesis 990; Clinical and Radiological Features, Lung Function Impairment and Assessment 991; Diagnostic Approach 993; Treatment 993; Prevention 994 97. Berylliosis 996 Clayton T Cowl Clinical and Radiological Features 996; Diagnosis 997; Treatment 998; Beryllium Exposure and Lung Cancer Risk 998: Prevention 999 98. The Health Risks of Asbestos Fiber Inhalation 1001 Jessica R Deslauriers, Harakh V Dedhia, Daniel E Banks Asbestos Fibers 1002; Asbestosis 1004; Medical Removal Protection/Exposure Prevention 1006; Asbestos Fibers and the Pleural Space 1006; Malignant Mesothelioma 1010; Lung Cancer 1012; Others Asbestos-related Cancers 1013; An Assessment of the Extent of Asbestos-related Disease in India 1013; Screening the Asbestos-exposed Worker for Lung Cancer 1014 99. Bronchial Anthracofibrosis 1019 Ashok Shah, Chandramani Panjabi, Vikas Pilaniya Bronchial Anthracofibrosis and Biomass Fuel Smoke Exposure 1019; Bronchial Anthracofibrosis and Tuberculosis 1024; Bronchial Anthracofibrosis and Other Respiratory Conditions 1024 100. Respiratory Disability 1027 Mahesh PA, Greeshma MV Impairment and Disability 1027; Clinical Approach to Respiratory Disability Evaluation 1028; History, Symptoms, Functional limitations, and Physical Examination 1028; Disability Assessment 1030; Disease-specific Impairment Evaluations 1033; Apportionment 1036; Workplace Protection 1036 1040 101. Occupational Asthma

Lt Col (Dr) Rahul Tyagi, Saurabh Mittal

Irritant-induced Asthma 1043

Economic Burden 1040; Occupational Asthma: Agents and Causation 1040; Diagnosis 1041;

102. High-altitude-related Illness 1045 Air Cmde Ajay Handa, Col Vikas Marwah, Lt Col (Dr) Robin Choudhary Physical Changes with Altitude 1045; Physiological Adaptation to High Altitude 1045; Altitude-related Specific Illnesses 1046; Effects of High Altitude on Existing Lung Diseases 1047 103. Aviation and Space Travel 1051 Air Cmde Ajay Handa, Lt Col (Dr) Rahul Tyagi Respiratory Physiology with Altitude 1051; Preflight Assessment 1051; Prescribing Inflight Oxygen 1053; COVID-19 and Air Travel 1053; Microgravity and Weightlessness 1054; Assessment Prior to Space Travel 1055 SECTION 10: DIFFUSE PARENCHYMAL INTERSTITIAL LUNG DISEASES 104. Diagnosis and Classification of Interstitial Lung Diseases 1059 Alok Nath, Zafar Neyaz Historical Aspect 1059; Classifications 1059; Diagnosis 1061; Future Directions 1071 105. Idiopathic Pulmonary Fibrosis 1074 Zein Kattih, Joseph Parambil, Stephen Machnicki, Suhail Raoof Pathogenesis of Idiopathic Pulmonary Fibrosis 1074; Idiopathic Pulmonary Fibrosis in India 1074; Clinical Manifestations 1074; Imaging Findings 1075; Histologic Features 1077; Multidisciplinary Discussion 1077; Monitoring of Clinical Progression 1078; Treatment and Management 1078; Acute Exacerbations of Idiopathic Pulmonary Fibrosis 1079 106. Interstitial Lung Disease other than Idiopathic Pulmonary Fibrosis 1082 Zein Kattih, Joseph Parambil, Arunabh Talwar, Stephen Machnicki, Suhail Raoof Pathogenesis of Interstitial Lung Disease 1082; Classification of Interstitial Lung Disease 1082; Epidemiology 1083; Clinical Manifestations 1083; Imaging Findings 1084; Diagnosis 1086; Treatment and Management 1087; Prognosis 1088; Acute Exacerbations of Interstitial Lung Diseases 1089 107. Interstitial Lung Abnormalities 1091 Zein Kattih, Hiroto Hatabu, Stephen Machnicki, Kevin K Brown, Suhail Raoof Definition and Classification of Interstitial lung abnormalities 1091; Incidence and Risk Factors 1092; Imaging 1092; Clinical Outcomes 1093; Disease Monitoring 1095 1097 108. Connective Tissue Disease-Interstitial Lung Disease Simon Meredith, Joseph Parambil, Kevin K Brown, Dominick Guerrero, Stephen Machnicki, Suhail Raoof Pathogenesis 1097; Rheumatoid Arthritis 1097; Systemic Sclerosis 1098; Idiopathic Inflammatory Myopathies 1098; Sjögren Syndrome and Mixed Connective Tissue Disease 1098; Treatment 1100; Idiopathic Interstitial Pneumonia with Autoimmune Features 1102 109. Connective Tissue Disease–Associated Interstitial Lung Diseases: **An Indian Perspective** 1107 Vijay Hadda, Sujay Halkur Shankar

Epidemiology 1107; Pathogenesis 1107; Natural History and Prognosis 1108; Approach to Diagnosis of CTD-

associated ILD 1109; Connective Tissue Disease Characteristics 1111; Management 1112

110.	Progressive Pulmonary Fibrosis Simon Meredith, Joseph Parambil, Suhail Raoof Definition 1117; Physiological Progression 1117; Radiological Progression 1117; Clinical Approach 1118; Prognosis 1119; Treatment 1119	1117
111.	Progressive Pulmonary Fibrosis: An Indian Perspective Sujeet Rajan, Rohit Joshi Definition 1123; Criteria for Progressive Pulmonary Fibrosis 1123; Treating Progressive Pulmonary Fibrosis 1124; Future Directions 1126	1123
112.	Organizing Pneumonia Brenda D Garcia, Diane Stover, Stephen Machnicki, Suhail Raoof Epidemiology 1128; Causes 1128; Clinical Features 1128; Algorithmic Approach to Diagnosis 1130; Differential Diagnosis 1132; Histology 1133; Treatment 1133; Monitoring/Prognosis 1134	1128
113.	Hypersensitivity Pneumonitis Ambika Sharma, Sheetu Singh, Kevin K Brown Epidemiology 1138; Etiopathogenesis 1138; Clinical Features 1139; Diagnostic Evaluation 1139; Disease Progression and Outcomes 1142; Management of Hypersensitivity Pneumonitis 1143; Prevention of Hypersensitivity Pneumonitis 1144	1138
114.	Radiation Pneumonitis: Radiation-induced Lung Injury Brenda D Garcia, Stephen Machnicki, AGabriella Wernicke Type of Radiation 1147; Epidemiology 1147; Mechanism of Lung Injury 1147; Risk Factors 1147; Signs and Symptoms 1148; Diagnosis 1148; Staging 1152; Grading by Imaging 1154; Treatment 1154; Prevention/Prophylaxis/Prediction 1155	1147
115.	Drug-induced Respiratory Diseases Kavitha Venkatnarayan, Uma Maheswari Krishnaswamy	1157
116.	Sarcoidosis Sahajal Dhooria History 1165; Epidemiology 1165; Risk Factors 1166; Pathogenesis and Immunology 1167; Pathology 1168; Clinical Features 1169; Diagnosis 1174; Treatment 1180; Prognosis and Mortality 1185; Future Directions 1185	1165
117.	Pulmonary Eosinophilic Disorders Aditya Jindal, Subhash Varma Eosinophils 1195; Pulmonary Eosinophilic Disorders 1196	1195
	SECTION 11: DISORDERS OF PULMONARY CIRCULATION	
118.	Diffuse Alveolar Hemorrhage F Karakontaki, E Stagaki, V Polychronopoulos	1209

Diagnostic Evaluation 1209; Antineutrophil Cytoplasmic Antibody 1212; Classification of Systemic Vasculitis 1212; Granulomatosis with Polyangiitis 1213; Microscopic Polyangiitis 1216; Eosinophilic

	Other Causes of Diffuse Alveolar Hemorrhage 1218	
119.	Pulmonary Hypertension: Etiology and Classification Radha Munje, Gyanshankar Mishra, Nikhil Rathod Definition of Pulmonary Hypertension 1221; Classification 1222; Pathophysiology 1223	1221
120.	Pulmonary Hypertension: Clinical Features and Diagnostic Evaluation Aditya Jindal Clinical Features 1227; Diagnostic Evaluation 1228	1227
121.	Pulmonary Hypertension due to Left Heart Disease Mateus Fernandes, Erica Altschul Definition 1232; Etiology 1233; Pathophysiology 1233; Clinical Presentation and Diagnosis 1234; Management 1236; Monitoring of PH-LHD 1238; Prognosis and Future Directions 1238	1232
122.	Pulmonary Hypertension due to Chronic Lung Disease (Group 3 Pulmonary Hypertension) Linda Benes, Himanshu Deshwal, Roxana Sulica Definition of Pulmonary Hypertension 1242; Definition of Group 3 Pulmonary Hypertension 1242	1242
123.	Management of Pulmonary Hypertension Trinath Dash, Karthik Tipparapu, K Arun Vishnu Supportive Therapies 1252; Specific or Targeted Therapies 1253; Combination Therapy Strategies 1255; Overall Therapeutic Strategy 1256	1252
124.	Pulmonary Thromboembolism Shona Arlin Christopher, Devasahayam J Christopher Epidemiology 1258; Definition 1258; Pathogenesis and Pathophysiology 1258; Risk Factors 1259; Clinical Features 1260; Diagnosis 1260; Management 1264; Risk Stratification in Acute Pulmonary Embolism 1268; Pulmonary Embolism Response Team 1269	1258
125.	Pulmonary Arteriovenous Malformations Matthew Kheir, Erica Altschul, Joseph Parambil Significance 1272; Etiology 1272; Epidemiology 1273; Pathology 1273; Clinical Manifestations 1273; Complications of Pulmonary Arteriovenous Malformation 1273; Diagnostic Workup 1274; Treatment and Management 1277; Follow-up 1278	1272

granulomatosis with Polyangiitis (Churg–Strauss Syndrome) 1217; Immunoglobulin A Vasculitis (Henoch–Schönlein Purpura) 1217; Isolated Pulmonary Capillaritis 1217; Vasculitis Associated with

Systemic Disease 1218; Anti-glomerular Basement Membrane Disease 1218;

SECTION 12: PLEURAL DISEASES

126. Pleura: Anatomy and Physiology

1283

Srinivas Rajagopala

Anatomy of the Pleura 1283; Development of the Pleural Membranes 1283; Histology of the Pleura 1283; Pleural Fluid: Normal Volume and Cellular Contents 1284; Physiology and Pathophysiology of Pleural Fluid Turnover 1284; Pleural Radiography and Ultrasound 1285

127.	Pleural Disorders Aditya Jindal Types of Pleural Diseases 1287; Diagnostic Approach to Pleural Diseases 1289; Treatment 1291	1287
128.	Parapneumonic Effusion and Empyema Devasahayam J Christopher, Priya N Definitions 1293; Risk Factors 1293; Pathogenesis 1293; Epidemiology 1294; Bacteriology 1294; Clinical Features and Diagnosis 1295; Pleural Fluid Analysis 1296; Treatment 1298	1293
129.	Tuberculous Pleural Effusion Dharmesh Patel, Radhika Banka Pathophysiology 1303; Clinical Features 1303; Diagnosis 1303; Treatment 1307	1303
130.	Malignant Pleural Effusions and Pleurodesis Srinivas Rajagopala Etiology of Malignant Effusions 1311; Pathogenesis of Metastasis and Effusions 1311; Clinical Presentation 1312; Radiological Findings 1312; Diagnosis 1313; Management 1315	1311
131.	Uncommon Pleural Effusions MS Barthwal, Sachinkumar S Dole Chylothorax 1321; Pseudochylothorax 1322; Meigs Syndrome 1323; Yellow Nail Syndrome 1323; Urinothorax 1324	1321
132.	Pneumothorax Uma Devaraj, Geroge D'Souza Definitions 1326; Pathophysiology 1326; Incidence 1327; Etiology 1327; Clinical Manifestations 1329; Laboratory Investigations and Diagnosis 1329; Recurrence Rates 1331; Treatment 1331; latrogenic Pneumothorax 1336; Traumatic (Noniatrogenic) Pneumothorax 1336; Tension Pneumothorax 1337	1326
133.	Tunneled Indwelling Pleural Catheter <i>George Mundanchira, Abhinav Agrawal, Viera Lakticova</i> Indications 1339; Tunneled Indwelling Pleural Catheter Placement 1340; Drainage Frequency 1341; Complications 1341; Removal 1341; Cost 1342	1339
S	ECTION 13: MEDIASTINUM, CHEST WALL AND DIAPHRAGM DISC	ORDERS
134.	Mediastinal Anatomy and Disorders Arjun Srinivasan, Surinder K Jindal Mediastinal Anatomy and Compartments 1347; Imaging of Mediastinum 1347; Pneumomediastinum 1348; Radiological Findings 1349; Differential Diagnosis 1349; Treatment and Clinical Course 1349; Mediastinitis 1350; Clinical Manifestations 1350; Management 1351	1347
135.	Diseases of the Chest Wall Balamugesh T Kyphoscoliosis 1358; Pectus Excavatum 1360; Pectus Carinatum 1361; Ankylosing Spondylosis 1361; Obesity 1362; Flail Chest 1363; Miscellaneous Conditions 1363	1358

136. Diseases of Diaphragm 1367 Balamugesh T Signs and Symptoms of Diaphragmatic Disorders 1367; Causes 1367; Diagnosis 1367; Management 1370; Disorders in the Structure of Diaphragm 1370 **SECTION 14: SYSTEMATIC DISEASES AND PREGNANCY** 137. Rare Lung Diseases 1377 Sanjeev Mehta, Bineet Ahluwalia Pulmonary Alveolar Phosphoproteinosis 1377; Pulmonary Calcification and Ossification Syndromes 1379; Pulmonary Alveolar Microlithiasis 1380 138. Diabetes Mellitus and Respiratory Disease 1383 Rajneesh Mittal Pathophysiology of Lung Dysfunction in Patients with Diabetes Mellitus 1383; Lung Infections 1383; Pulmonary Tuberculosis 1384; COVID-19 Infection 1384; Chronic Obstructive Pulmonary Disease 1385; Bronchial Asthma 1385; Obstructive Sleep Apnea 1385; Lung Cancer 1385; Cystic Fibrosis 1386; Acute Lung Injury/Acute Respiratory Distress Syndrome 1386; Idiopathic Pulmonary Fibrosis 1386; Lung Diseases and Antidiabetic Drugs 1386 139. Pulmonary Disease in Pregnancy 1389 **Umesh N Jindal** Maternal Respiratory Adaptation 1389; Respiratory Physiology During Pregnancy 1389; Lung Perfusion 1390; Ventilation 1390; Blood Gases 1390; Cardiovascular System 1391; Common Clinical Symptoms and Other Issues 1391 140. Respiratory Drugs during Pregnancy 1400 Manishi Mittal Safety Concerns 1400 141. Oxygen Therapy in Critically III Pregnant Women 1416 Mohankumar Thekkinkattil Definition 1416; Importance of Oxygen Therapy in Critically III Pregnant Women 1416; Evidence for Oxygen Therapy During Pregnancy 1418 **SECTION 15: RESPIRATORY SLEEP DISORDERS** 142. Sleep-related Respiratory Disorders 1423 Sean Michael Duenas, Harly Greenberg Obstructive Sleep Apnea 1423; Central Sleep Apnea 1427; Nocturnal Hypoventilation Syndromes 1429 143. Obstructive Sleep Apnea-Hypopnea Syndrome 1433 Harmanjit Singh Hira, Naresh Kumar Definition 1433; Pathophysiology 1433; Clinical Features 1434; Physical Examination 1434; Causes 1434;

Laboratory Investigations 1435; Treatment 1436; Prognosis 1439; Patient Education 1439; Special Concerns 1439

144.	Obstructive Sleep Apnea Syndrome Comorbidities Dipti Gothi, Sunil Kumar	1442
	Metabolic and Systemic Comorbidities 1442; Obstructive Sleep Apnea and Respiratory Comorbidity 1444; Sleep Comorbidities 1445; Obesity Hypoventilation Syndrome 1446	
145.	Nocturnal Limb Movement Disorders	1451
	Kevin Shayani, Jacob Schwartz, Margarita Oks	
	Epidemiology and Risk Factors 1451; Pathophysiology 1451; Clinical Features 1452; Diagnosis and Differential Diagnosis 1452; Treatment 1453	
146.	Rapid Eye Movement Behavior Sleep Disorder	1455
	Kevin Shayani, Margarita Oks	
	Epidemiology 1455; Pathogenesis 1455; Etiology 1455; Clinical Features 1456; Diagnosis 1456; Differential Diagnosis 1458; Management 1458; Prognosis 1459	
147	Insomnia	1461
177.	Eby Thekkedath, Margarita Oks	1401
	Classifications 1461; Epidemiology and Etiology 1461; Signs and Symptoms 1462;	
	Pathophysiology 1462; Evaluation and Diagnosis 1463; Management 1464; Other Disease Associations 1466; Effects on Other Physiologic Systems 1467	
148.	Pediatric Obstructive Sleep Apnea	1470
	Unnati Desai, Jyotsna M Joshi	
	Definition 1470; Etiology 1470; History and Clinical Examination 1471; Management of Obstructive Sleep Apnea in Children 1472	
	SECTION 16: LUNG NEOPLASMS	
149.	Epidemiology and Risk Factors of Lung Cancer	1477
	Deepak Aggarwal, Komaldeep Kaur	
	Epidemiology of Lung Cancer 1477; Lung Cancer Epidemiology in India 1477; Lung Cancer in Never Smokers 1478; Risk Factors of Lung Cancer 1478	
150.	Lung Cancer: Clinical Manifestations	1484
	Javid Ahmad Malik	
	Local Manifestations 1484; Metastatic Manifestations 1485; Endocrine Syndromes 1490; Syndrome of Inappropriate Antidiuretic Hormone 1491; Neurological Syndromes 1491; Hematological Syndromes 1492; Skeletal 1493; Miscellaneous Syndromes 1493	
151.	Staging and Management Decisions of Lung Cancer	1495
	Pawan Singh, Aman Ahuja	
	Descriptors 1495; Pathological Staging 1495; Pitfalls of Current Staging 1498; Management Options 1498; Management Decisions Based on Staging 1499	

152.	Approach to Management of Lung Cancer in India	1501
	Sudhir Kumar, Neha Pathak	
	Clinical Presentation 1501; Diagnosis and Staging 1501; Histopathology 1503; Role of the Multidisciplinary Approach 1504; Stage-wise Management of Lung Cancer 1504	
153.	Targeted Therapy in Lung Cancer	1510
	Puneet Saxena, Itishree Singh, Pawan Singh, Anvesh Rathore	
	Driver versus Passenger Mutations 1510; Epidermal Growth Factor Receptor Mutations 1510; Anaplastic Lymphoma Kinase Rearrangements 1513; <i>ROS1</i> Rearrangements 1514; Mesenchymalepithelial Transition Factor Abnormalities 1514; V-RAF Murine Sarcoma Viral Oncogene Homolog B1 Mutations 1515; Neurotrophic Tropomyosin Receptor Kinase Fusions 1515; Rat Sarcoma Mutations 1515; HER2 Mutations and Amplifications 1516; Targeted Therapy in Early-stage Lung Cancer 1516	
154.	Solitary Pulmonary Nodule	1519
	Alladi Mohan, B Vijayalakshmi Devi, Abha Chandra	
	Terminology 1519; Epidemiology 1519; World Scenario 1519; India 1520; Etiology 1520; Clinical Evaluation 1520; Predicting the Risk of Malignancy in Solitary Pulmonary Nodule 1521; Imaging Studies 1521; Tissue Sampling Techniques 1527; Management 1528	
155.	Hematopoietic and Lymphoid Neoplasm of Lungs	1531
	Charanpreet Singh, Gaurav Prakash, Pankaj Malhotra	
	Lymphomas 1531; Secondary Lung Involvement in Hodgkin Lymphoma 1533; Secondary Involvement of Lung by Other Systemic Hematopoietic and Lymphoid Disorders 1535; Plasma Cell Dyscrasias 1536; Posttransplant Lymphoproliferative Disorders 1536; Chemotherapeutic Drugs Lung Toxicity 1536; Miscellaneous Mechanisms of Pulmonary Involvement 1536	
156.	Lung Cancer Screening	1540
	Mateus Fernandes, Viera Lakticova, Brett Bade, Suhail Raoof	
	Benefits of Screening 1540; Screening Considerations and Associated Risks 1542; Integrating Smoking Cessation in Lung Cancer Screening 1544; Adherence 1544; Risk Assessment Tools 1544; Shared Decision-making 1545; Managing Screen-detected Lung Nodules 1545	
157.	Lung Cancer Screening: An Indian Perspective	1549
	Vikram Damaraju, Adimulam Ganga Ravindra	
	Screening 1549; Risk Factors for Lung Cancer 1549; Modes of Screening: Chest Radiography and Sputum Cytology 1549; Low-dose Computed Tomography 1550	
	SECTION 17: RESPIRATORY CRITICAL CARE	
158.	Clinical Approach to Hypoxia	1561
150.	Aloke Gopal Ghoshal, Angira Dasgupta, Avik Ghoshal	1301
	Journey of Oxygen 1561; Development of Hypoxia and Hypoxemia 1562; Causes of Hypoxia 1563; Approach to Hypoxia 1565	
159.	High-flow Nasal Cannula Oxygen	1567
1 2 2 .	Amit Mandal	1507
	Mechanism of Action and Physiological Effects 1567; Clinical Indications 1567; Benefits of High-flow	

Evidence and Research 1569

160.	Noninvasive Ventilation GC Khilnani, Vijay Hadda	1571
	Technical Aspect of Noninvasive Ventilation 1571; Steps to Successful Provision of Noninvasive Positive Pressure Ventilation 1574; Clinical Uses of Noninvasive Positive Pressure Ventilation: Evidence and Recommendations 1575; High-flow Nasal Cannula versus Noninvasive Ventilation 1578	
161.	Mechanical Ventilation: General Principles and Modes	1582
	GC Khilnani, Vijay Hadda	
	Indications of Mechanical Ventilation 1582; Basic Aspects of Mechanical Ventilation 1582; Modes of Mechanical Ventilation 1584; Newer Modes of Mechanical Ventilation 1589; Initiating Mechanical Ventilation 1592; Complications of Mechanical Ventilation 1595	
162.	Respiratory Failure	1598
	Abinash Sherindar Singh Paul, Ritesh Agarwal	
	Classification 1598; Mechanisms of Respiratory Failure 1599; Clinical Manifestations of Respiratory Failure 1600; Diagnosis 1600; Treatment 1601	
163.	Acute Respiratory Distress Syndrome: Epidemiology, Etiology,	
	Pathophysiology, Definition, and Subphenotypes	1607
	Valliappan Muthu, Kuruswamy Thurai Prasad, Ritesh Agarwal	
	Epidemiology of Acute Respiratory Distress Syndrome 1607; Definition of Acute Respiratory Distress Syndrome 1607; Precipitating Causes of Acute Respiratory Distress Syndrome 1610; Pathophysiology of Acute Respiratory Distress Syndrome 1610; Subphenotypes of Acute Respiratory Distress Syndrome 1612	
164.	Acute Respiratory Distress Syndrome: Respiratory Mechanics, Management, and Long-term Outcomes	1616
	Valliappan Muthu, Inderpaul Singh Sehgal, Ritesh Agarwal	
	Applied Respiratory Mechanics 1616; Practical Aspects of Mechanical Ventilation 1617; Management of Refractory Hypoxemia 1619; Long-term Outcome of Acute Respiratory Distress Syndrome 1621	
165.	Sepsis and Septic Shock	1625
	Dhruva Chaudhry, Lokesh Kumar Lalwani	
	Definition 1625; Phenotypes of Sepsis 1626; Risk Factors and Etiology of Sepsis 1626; Pathogenesis of Sepsis 1627; Management of Sepsis and Septic Shock 1628; Post-sepsis Syndrome 1632	
166.	Nonpulmonary Critical Care I	1635
	Liziamma George, Ivan Wong	
	Gastrointestinal and Hepatic Problems in Critical Care 1635	
167.	Nonpulmonary Critical Care II (Hematological and Renal Problems)	1647
107.	Liziamma George, Ivan Wong	1047
	Anemia 1647; Thrombocytopenia 1649; Thrombotic Thrombocytopenic Purpura 1651; Risks of Transfusion 1651;	
	Coagulopathy in the Intensive Care Unit 1651; Acute Kidney Injury 1652; Prevention of Acute Kidney Injury 1655	
168.	Nonpulmonary Critical Care III (Endocrinal and Neurological Problems)	1657
	Liziamma George, Ivan Wong	
	Thyroid Storm 1657; Myxedema Coma 1658; Acute Adrenal Insufficiency 1658; Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State 1659; Acute Ischemic Stroke 1663;	

Subarachnoid Hemorrhage 1667; Intracerebral Hemorrhage 1669; Status Epilepticus 1671

169.	Toxic Inhalations Clayton T Cowl	1675
	Physical Properties of Gases as a Diagnostic Tool 1676; Pathophysiology of Acute Toxic Inhalation Injury 1676; Estimating Clinical Severity in Acute Toxic Lung Injury 1677; Respiratory System Effects from Specific Inhaled Toxicants 1677	
170.	Pulmonary Arterial Hypertension in the Intensive Care Unit	1683
	Himanshu Deshwal, Linda Benes, Roxana Sulica	
	Pathophysiology of Right Heart Failure in Pulmonary Hypertension 1683; Pulmonary Hypertension in the Critically III Patient 1684; Management 1687; Management of Respiratory Failure in PAH in ICU 1691	
171.	Hemodynamic Monitoring in Intensive Care Unit	1695
	Rajkalyan Chakrabarti, Purvesh R Patel, Pralay K Sarkar	
	Conceptual Framework of Hemodynamic Monitoring and Management 1695; Clinical and Laboratory Measures of Tissue Perfusion 1695; Measurement of Pressure Using Fluid-filled Systems 1696; Systemic Blood Pressure Measurement 1697; Central Venous Pressure and Right Atrial Pressure Monitoring 1701; Right Heart/Pulmonary Artery Catheterization 1702; Advanced Critical Care Echocardiography in Hemodynamic Monitoring 1706; Measurement of Cardiac Output 1711; Application of Hemodynamic Data 1719	
172.	Right Heart Catheterization	1730
	Parmeet Saini, Vishal K Patel, Albina Guri, Anthony Saleh	
	Setup 1731; Insertion 1732; Interpretation 1732; Complications 1735; Clinical Controversy 1736	
173.	Role of Ultrasonography in Critical Care Medicine	1740
	Pralay K Sarkar, Seth J Koenig, Paul H Mayo	
	Training in Critical Care Ultrasonography 1741; Technical Considerations 1743; Thoracic Ultrasonography 1748; Critical Care Echocardiography 1759; Abdominal Ultrasound: Scope in Intensive Care Unit 1770; Ultrasound Assessment of Venous Thromboembolism 1775; Ultrasound Guidance for Procedures 1777	
174.	Sedation, Analgesia, and Delirium in the Intensive Care Unit	1791
	Karan Madan, Ayush Goel, Ritesh Agarwal	
	Assessment of Pain, Sedation, and Agitation in the Intensive Care Unit 1791; The Ideal Sedative Agent 1794; Opioid Analgesics 1794; Sedative Medications 1795; Choosing the Appropriate Sedative Agent 1797; Delirium 1797; The ABCDEF Bundle Approach 1799	
175.	Weaning from Mechanical Ventilation	1802
	Ajmal Khan	
	Types of Weaning 1802; Pathophysiology of Weaning 1803; Process of Weaning 1804	
176.	Hyperbaric Oxygen Therapy	1810
	PS Tampi	
	Rationale of Hyperbaric Oxygen 1810; Other Physiological Effects of Hyperbaric Oxygenation 1810; Beneficial Effects of Hyperbaric Oxygen 1811; Mechanism of Action of Hyperbaric Oxygen 1811; Indications 1811; Contraindications 1813; Complications 1813; Hyperbaric Oxygen in Pediatric Age Group 1814; Potential New Indications 1814; Hyperbaric Chambers 1814; Other Chambers 1815; Techniques of Hyperbaric Oxygenation 1815; World Distribution of Hyperbaric Chambers 1815; Hyperbaric Chambers in India 1815	

SECTION 18: SURGICAL ASPECTS

177. Surgical Management of Pneumonia

1819

Avantika Nathani, Pratibha G Gogia, Dean Schraufnagel, Atul C Mehta

Modern Indications 1819; Preoperative Assessment and Optimization 1826; Types of Procedures 1827; Postoperative Management and Complications 1827

178. Preoperative Evaluation

1829

Mahesh PA, Greeshma MV, Jayaraj BS

Importance of Preoperative Assessment 1829; Perioperative Risk Assessment 1829; Risk Factors 1831; Role of Preoperative Tests 1831; Strategies to Minimize Perioperative Pulmonary Risk 1836

179. Lung Transplantation

1839

Kuruswamy Thurai Prasad, Ritesh Agarwal

History 1839; Candidate Selection, Evaluation, and Management 1839; Waiting List and Organ Allocation 1844; Donor Selection, Evaluation, Matching, and Harvesting 1844; Surgery and Postoperative Care 1846; Immunosuppression and Prophylactic Therapy 1846; Follow-up 1847; Complications 1847; Outcomes 1852; Lung Transplantation in India 1852

SECTION 19: PERSPECTIVES OF RESPIRATORY CARE

180. Ethics in Respiratory Care

1857

Basil Varkey

Meaning and Scope of Ethics 1857; Fundamental Principles of Ethics 1857; Conflicts between Principles 1860; Education and Challenges with Technological Advances 1863; A New Covenant for Physicians 1864; A Conceptual Model for Patient Care 1864

181. Psychosocial Aspects of Respiratory Diseases

1868

Kranti Garg, Nitin Gupta

Common Lung Diseases 1868; Assessment of Baseline Mental Health by the Pulmonologist 1869; A Brief Overview of Mental Health in Respiratory Diseases 1870; Multimorbidities 1871; Variable Patient Responses and Coping Mechanisms 1871; Psychological Distress and Caregivers 1871; Screening Tools for Stigma and Self-esteem, Psychological Distress, and HRQoL 1872; Pulmonologist versus Psychiatrist 1874; Indian Scenario 1874

182. End-of-Life Care

1877

Jenifer Jeba S. Jvothsna Kuriakose

Challenges with Prognostication 1877; Principles of Best Care for the Dying Person 1878; Steps of End-of-life Care Process 1878; Recognition of the Dying Process 1878; Common Symptoms at End-of-life 1879; Palliative Sedation 1883; Reviewing Medications at End-of-life 1884; Anticipatory Prescribing at the End-of-life 1884; Artificial Nutrition and Hydration at the End-of-life 1884; Application of Ethical Principles in End-of-life Care 1884; End-of-life Care in the Intensive Care Unit 1885; Provision of End-of-life Care in the Indian subcontinent 1885; Communication 1885; Support to the Caregivers 1885; Bereavement 1886

183. Health Economics of Pulmonary Care

1889

Sudheendra Ghosh C, Sayujya S Ghosh

Healthcare Market and Public Health 1889; Appraisal of the Evidence 1889; Perspective of the Analysis (Who Pays and Who Gains?) 1890; Types of Costs Involved 1890; Measures for Evaluating Outcomes and Quality of life 1890; Measure of Health-related Quality of Life 1891; Incremental Cost-effectiveness Ratio 1891; Economics of Chronic Obstructive Pulmonary Disease and Interstitial Lung Diseases 1892; Incremental Cost-effectiveness Ratio in COVID-19 (Remdesivir and Dexamathazone) 1892; Cost-effectiveness of Interventional Pulmonary Procedures 1892

SECTION 20: APPENDICES

Appendix A: Algorithmic Approach to Respiratory Diseases

1897

Appendix A.1: Bronchiolar Disorders Algorithm 1897; Appendix A.2: Cavitary Lung Disease Algorithm 1898; Appendix A.3: Cystic Lung Disease 1899; Appendix A.4: Lung Hyperlucency: Algorithmic Approach for Interpretation 1901; Appendix A.5: Pictorial Essay: Multinodular Disease 1902; Appendix A.6: Organizing Pneumonia: Algorithmic Approach 1904

Appendix B: From Our Archives of 1970s-1980s

1906

Index 1911

Oxygen Transport and Tissue Oxygenation

CHAPTER

Surinder K Jindal

armaer k Jinaar

INTRODUCTION

The delivery of oxygen to the tissues for cellular metabolism is a three-step process: (1) Oxygen consumption $(\dot{V}O_2)$ in the lungs (i.e., external respiration), (2) oxygen transport through the blood to the tissues, (3) diffusion of oxygen from the capillaries to the cells (i.e., internal respiration or tissue oxygenation).

OXYGEN TRANSPORT

Oxygen is transported in the blood bound to hemoglobin (Hb), a protein comprised of four subunits, two alpha subunits, and two beta subunits. Each Hb molecule can bind four oxygen molecules, forming oxyhemoglobin. The quantity of oxygen bound to Hb is dependent on the partial pressure of oxygen. The sigmoidal S-shape curve representing the content of oxygen in blood at various partial pressures of oxygen is called the oxygen-dissociation curve (Fig. 1). There is a steep slope at low partial pressures of oxygen and a more gradual slope at higher partial pressures. The affinity of Hb for oxygen results in a shift in the oxygen-hemoglobin dissociation curve. An increase in oxygen affinity results in the curve shifting to the left, whereas a decrease in oxygen affinity results in the curve shifting to the right (Fig. 1). The affinity of Hb for oxygen is affected by various factors (Table 1).

Tissue oxygenation is the final step in the *oxygen cascade*; it occurs when oxygen molecules delivered to the tissues enter the cells. The process of diffusion from the capillaries to the tissues is sometimes called *internal respiration*. The oxygen is consumed by the tissues for energy production (aerobic respiration) which is a far more effective method than the anaerobic glycolysis.

The main determinant of tissue oxygenation is a balance between oxygen delivery $(\dot{D}O_2)$ and $\dot{V}O_2$. An imbalance between the two results in oxygen debt. Both $\dot{D}O_2$ and $\dot{V}O_2$ depend upon several factors which can be differently influenced in health and disease (Box 1 and Table 2).

OXYGEN DELIVERY

Oxygen delivery constitutes the total amount of oxygen delivered to the whole body. Tissue $\dot{D}O_2$ depends on two factors: (1) Arterial O_2 content (CaO₂) and (2) cardiac output (Q), $\dot{D}O_2 = Q \times CaO_2$.

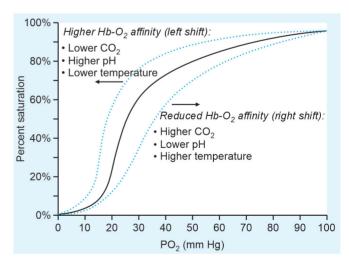


FIG. 1: Oxygen dissociation curve.

TABLE 1: Factors which affect the Hb affinity for oxygen.		
Factor	Effect of increase	Effect of decreased level
 pH (Increased H⁺/pCO₂) 	Affinity for O ₂ increases (Bohr effect)	Affinity for O ₂ decreases (Bohr effect)
 2,3-diphosphoglycerate (2,3-DPG) 	Decreases the Hb affinity	Increases affinity
Temperature	Decreases the affinity	Increases affinity

The normal range for $\dot{D}O_2$ is 520–570 mL/min/m² and under normal physiological conditions, $\dot{D}O_2$ is considerably in the excess of $\dot{V}O_2$ (110–160 mL/min/m²). This "spare capacity" enables the body to cope with a fall in $\dot{D}O_2$ without initially compromising aerobic respiration.

■ Factors Influencing Oxygen Delivery

Arterial O₂ Content

Arterial O_2 content (Ca O_2) is the total amount of O_2 present in blood, i.e., combined with Hb and dissolved in plasma.

$$CaO_2 = (1.34 \times Hb \times SaO_2) + (0.0031 \times PaO_2)$$

The contribution of Hb is described by the first part of the equation. This relationship states that each gram of Hb will bind 1.34 mL of O_2 , when it is fully saturated with oxygen. The SaO₂ is expressed as a fraction, not a percentage (i.e., 1.0

BOX 1 Factors affecting $\dot{D}O_2$ and $\dot{V}O_2$.

Factors affecting DO

- Arterial O2 content:
 - Hemoglobin
 - Arterial oxygen saturation and PaO₂
- Cardiac output, depends upon:
 - o Preload
 - o Afterload
 - Cardiac contractility

Factors affecting $\dot{V}O_2$

- Causes of decreased VO₂:
 - Decreased blood supply to tissues: Shock (cardiogenic/ hypovolemic)
 - Cytotoxicity
 - o Increased O₂ demand, e.g., sepsis, acute pancreatitis, burns
- Causes of Increased VO₂:
 - Stress or tissue injury
 - Fever, tachypnea, shivering, and seizures

instead of 100%). Therefore, at a Hb level of 15 g/dL and an SaO_2 of 98%, the oxygen carried by Hb will be:

$$1.34 \times 15 \times 0.98 = 19.7 \text{ mL}/100 \text{ mL}.$$

From the second part of the equation, one can infer that at a PaO_2 of 100 mm Hg, the expected concentration of dissolved O_2 in blood is $0.0031 \times 100 = 0.3$ mL/100 mL. Therefore, the total concentration of O_2 in arterial blood is 19.7 + 0.3 = 20 mL/100 mL. Thus, it is clear that CaO_2 primarily depends on Hb and SaO_2 and to a lesser extent on PaO_2 .

Cardiac Output

 $\dot{\rm DO}_2$ is directly related to changes in cardiac output, which is the product of heart rate and stroke volume. Any alteration in either of these two parameters alters the cardiac output. Stroke volume, the amount of blood ejected per beat is affected by the following factors:

- *Preload:* It is the load imposed on a muscle before the onset of contraction and is synonymous with the initial length (or stretch) of cardiac fibers. An increase in preload augments muscle length and leads to a more forceful cardiac contraction (Frank-Starling phenomenon). In fact, in the normal heart, the diastolic volume/ preload is the principal force that governs the strength of ventricular contraction. This emphasizes the value of avoiding hypovolemia and correcting volume deficits promptly when they exist. The relationship between preload and cardiac output is, however, not linear and is also influenced by changes in ventricular compliance and geometry. Since ventricular end-diastolic volume is not easily measured at the bedside, end-diastolic pressure (EDP) and central venous pressure (CVP) are more commonly used as reflections of preload in clinical
- Afterload: It is the sum of all forces opposing ventricular ejection. It is influenced by aortic and pulmonary arterial pressures, systemic and pulmonary vascular resistance, and compliance of ventricular muscle. As the determination of these forces is complex, systolic

TABLE 2: Normal values and equations of tissue oxygenation parameters.		
Parameter	Equation	Normal range
Arterial O ₂ content (CaO ₂)	$(1.34 \times Hb \times SaO_2) + (0.0031 \times PaO_2)$	20 mL/dL
Cardiac output (Q)	hr×sv	4–8 L/min
Cardiac index (CI)	Q/BSA	2.4–4.0 L/min/m ²
Oxygen delivery (DO ₂)	$Q \times 1.34 \times Hb \times SaO_2$	900-1,000 mL/min
Oxygen delivery index (DO ₂ index)	DO ₂ /BSA	520-570 mL/min/m ²
Oxygen consumption ($\dot{V}O_2$)	$Q \times 1.34 \times Hb \times (SaO_2 - SvO_2)$	180-280 mL/min/m ²
Oxygen consumption index ($\dot{V}O_2$ index)	VO ₂ /BSA	110–160 mL/min/m ²
Oxygen extraction ratio (O ₂ ER)	$(SaO2 - SvO2/SaO2) \times 100$	20–30%
(BSA: body surface area; Hb: hemoglobin; hr: heart rate; PaO ₂ : partial pressure of O ₂ in arterial blood; SaO ₂ : arterial O ₂ saturation; SvO ₃ : mixed ver		

(BSA: body surface area; Hb: hemoglobin; hr: heart rate; PaO_2 : partial pressure of O_2 in arterial blood; SaO_2 : arterial O_2 saturation; SvO_2 : mixed venous O_2 saturation; SvO_2 saturation O_2 saturation O_2 saturation O_2

left ventricular pressure is usually used as a reasonable measure of afterload. In addition, since afterload is a transmural force, it is influenced by the pleural pressures at the surface of the heart. Positive pleural pressures can promote ventricular emptying by facilitating the inward displacement of the ventricular wall during systole, and this is one of the mechanisms by which noninvasive positive-pressure ventilation is beneficial in cardiogenic pulmonary edema.

Contractility: It refers to the intrinsic contractile property
of cardiac myocytes and is influenced by catecholamine
levels, as well as extracellular calcium concentration.
Cardiac contractility is measured indirectly by impedance cardiography and Doppler echocardiography.

The delivery of O_2 to the cells, i.e., the cellular O_2 supply is not equal to all cells although all arteries in the body carry virtually identical concentrations of O_2 . This is because of the following factors:

- Differences in regional blood flow: The gatekeeper of blood supply to a capillary network is the local arteriole. Arterioles may dilate or constrict in response to various local and central regulatory factors. Local factors causing dilatation include hypoxia, increased CO₂, increased temperature, and decreased pH. The release of catecholamines is a central mechanism that attempts to preferentially distribute blood to vital organs when $\dot{D}O_2$ is compromised. When the body is confronted with a declining $\dot{D}O_2$, both central and local mechanisms are stimulated. In the short term, central effects predominate while if the O_2 shortage persists, local effects override and generalized vasodilatation occurs.
- Differences in capillary architecture: Some cells are simply closer to capillaries than others. Because movement of O₂ depends on pressure gradients, the cells farthest away from capillaries are most vulnerable to hypoxia. In addition, many capillaries are normally closed and open only when perfusion to that particular region increases. For example, an actively contracting muscle may have 10 times more open capillaries than a resting muscle.

OXYGEN CONSUMPTION

Oxygen consumption refers to the rate of uptake of $\rm O_2$ by tissues from microcirculation. It is a product of the cardiac output and the difference in oxygen content between arterial and venous blood.

 $\dot{\mathbf{V}}\mathbf{O}_2 = Q \times (\mathbf{CaO}_2 - \mathbf{CvO}_2) \,\dot{\mathbf{V}}\mathbf{O}_2 = Q \times 1.34 \times \mathbf{Hb} \times (\mathbf{SaO}_2 - \mathbf{SvO}_2)$

The normal range for $\dot{V}O_2$ is 110–160 mL/min/m².

Measurement of Oxygen Consumption

 $\dot{V}O_2$ can be measured in three ways:

1. Using Fick's equation (as above). It requires the placement of a pulmonary artery catheter.

- 2. By measurement of inspired and expired minute ventilation (Vi and Ve) and of fractional concentrations of O_2 (FiO₂ and FeO₂) in the two samples. This is a noninvasive method but is relatively unreliable in mechanically ventilated patients on high FiO₂. $\dot{V}O_2 = (Vi \times FiO_2) (Ve \times FeO_2)$
- 3. \dot{V} O₂ can also be measured directly with the help of a rebreathing spirometer system filled with oxygen; the expired CO₂ is absorbed from the system and any change in the volume of gas in the spirometer reflects the \dot{V} O₂.

Cellular O_2 utilization: Metabolic utilization of O_2 in cells occurs by the oxidation of pyruvic acid in the Krebs cycle. This series of reactions takes place in mitochondria and results in the production of 38 molecules of adenosine triphosphate (ATP). The availability of O_2 is crucial in the production of ATP from adenosine diphosphate (ADP) in the Krebs' cycle. The actual process of ATP formation is called oxidative phosphorylation as phosphate is added to ADP by using the energy from oxidation. In the absence of O_2 , metabolism is less efficient and only 2 molecules of ATP are generated by the metabolism of glucose (anaerobic glycolysis). Furthermore, anaerobic metabolism results in the production of lactic acid, which may lead to systemic metabolic acidosis.

More than 90% of the body's $\dot{V}O_2$ is utilized by a single enzyme, cytochrome oxidase, during the process of oxidative phosphorylation, which generates ATP. This is the most efficient means of producing ATP, since a total of 38 molecules of ATP are generated per molecule of glucose. Aerobic cellular respiration depends on the efficient supply of oxygen to the mitochondria, which is a function of the coordinated interaction between the respiratory and circulatory systems. When oxygen supply is inadequate, anaerobic metabolism sets in and generates only 2 molecules of ATP per molecule of glucose. In addition H⁺ ions are formed, which can lead to a systemic metabolic acidosis. Tissue oxygenation is often impaired in critically ill patients, who have poor cardiopulmonary reserve and optimizing DO₂ to meet oxygen demand, has the potential to improve outcomes in these patients.

Calculated versus Measured Oxygen Consumption (VO₂)

 $\dot{V}O_2$ is usually derived from Fick's equation and not directly measured. The derivation is based on four measured variables: Cardiac output (Q), hemoglobin concentration (Hb), arterial O_2 saturation (SaO $_2$), and mixed venous O_2 saturation (SvO $_2$). Each of these measurements varies and their summed contribution can lead to considerable variability in the final calculated \dot{V} O_2 . Therefore, to be considered a physiologically significant change, the calculated $\dot{V}O_2$ should change by at least 15%.

OXYGEN EXTRACTION RATIO

Oxygen extraction ratio (O_2ER) is the ratio of oxygen consumption to oxygen delivery $(\dot{V}O_2/\dot{D}O_2)$ and reflects the fraction of O_2 delivered to the microcirculation that is taken up by the tissues. The O_2ER varies between different organs. For example, the brain has an O_2ER of 34% while exercising muscle can remove all O_2 from its microcirculation and thus have an O_2ER approaching 100%. Overall, the normal O_2ER is 20–30%. Thus, only a small fraction of the available O_2 delivered to the capillaries is taken up into the tissues. Oxygen extraction is adjustable, and in conditions where O_2 delivery is impaired, the O_2ER can increase up to 50–60%.

OXYGEN DELIVERY-OXYGEN CONSUMPTION CURVE

The relationship between DO₂ and VO₂ is described by the curve in **Figure 2**. As DO₂ decreases below normal, the O₂ER increases proportionally to keep VO₂ constant. When O₂ER reaches its maximum level (50-60%), further decreases in DO₂ result in proportional decreases in VO₂. Since under normal physiological conditions, DO₂ is considerably in excess of the VO2, tissue oxygenation to a large extent is supply independent. However, when DO₂ falls below a certain critical level, VO₂ becomes supply dependent and this condition, in which cellular metabolism is limited by the supply of O₂, is called dysoxia. This critical O₂ delivery point (critical DO₂) varies between 150 and 1,000 mL/min/m² in critically ill patients, though on an average it is approximately 300 mL/min/m². When DO₂ falls below this level, tissue hypoxia ensues, blood lactate increases, and prognosis becomes poor. Thus, maintenance of DO2 in excess of the

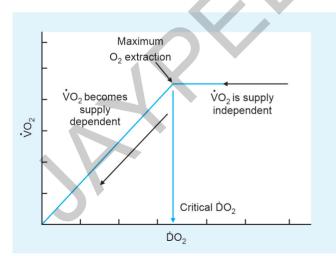


FIG. 2: Graph describing the relationship between oxygen delivery $(\dot{D}O_2)$ and O_2 consumption $(\dot{V}O_2)$. As $\dot{D}O_2$ decreases below normal, O_2 extraction increases proportionally to keep $\dot{V}O_2$ constant and therefore is "supply independent". When $\dot{D}O_2$ falls below a critical level, $\dot{V}O_2$ becomes "supply dependent".

critical delivery point is crucial in the management of critically ill patients. This is particularly true when positive endexpiratory pressure (PEEP) is being used because PEEP may be associated with a fall in $\dot{D}O_2$ despite improvements in PaO₂ because of its effect on cardiac output.

Factors Influencing Oxygen Consumption

- Causes of decreased VO₂:
 - Decreased blood supply to tissues: Shock (cardiogenic/ hypovolemic).
 - Cytotoxicity: An intrinsic defect in O₂ utilization at the cellular level is seen in carbon monoxide and cyanide poisoning, as well as in sepsis,
 - o Increased O_2 demand: This is seen in most critically ill patients with increased metabolic rates, e.g., acute pancreatitis and burns. It is noteworthy that tissue hypoxia in sepsis involves all the three mechanisms mentioned above: (1) Decreased blood supply as a result of redistribution of blood flow due to pathologic capillary dilatation and arteriovenous shunting, as well as microvascular occlusion due to platelet and fibrin microthrombi; (2) disruption of cellular metabolism by cytokines and free radicals; and (3) increased O_2 demand.
- Causes of increased $\dot{V}O_2$: Whenever stress or tissue injury occurs, there is an increase in metabolic rate and $\dot{V}O_2$. In normal subjects, exercise increases $\dot{V}O_2$, almost simultaneously with the onset of work. Most of this increase is accounted for by an increase in cardiac output. A relative hemoconcentration and therefore increased O_2 content may also occur with the high levels of exercise. The $\dot{V}O_2$ may increase 10–15-fold during exercise. In addition, O_2 extraction (see above) may also increase to as much as 80% of $\dot{V}O_2$ in order to meet the additional O_2 requirement. This is made possible by capillary dilatation and recruitment in exercising muscles.

Causes of increased $\dot{V}O_2$ in sick patients include fever, tachypnea, shivering, and seizures. In a very ill patient, even innocuous activities, such as chest physiotherapy, getting up or turning in bed, and tracheal suctioning, can increase $\dot{V}O_2$ and tilt the already precarious O_2 balance.

Oxygen Debt (VO₂ Deficit)

Oxygen debt or $\dot{V}O_2$ deficit is the difference between the metabolic demand for O_2 and the actual $\dot{V}O_2$. As demand increases, $\dot{V}O_2$ must increase to preserve aerobic metabolism. This is met with by increasing $\dot{D}O_2$ either by physiological compensation, e.g., an increase in cardiac output or O_2ER , or by therapeutic interventions, such as intravenous fluids or inotropes. If this increase in $\dot{D}O_2$ is delayed, O_2 debt continues to grow and a stage is reached from where recovery is not possible. Studies of the O_2 debt after resuscitation from

hemorrhagic shock and in postoperative patients show a direct relationship between the magnitude of $\rm O_2$ debt and the risk of multiorgan failure and death. This indicates that the early correction of $\rm \dot{V}O_2$ deficits is warranted to limit the severity of tissue ischemia.

ASSESSMENT OF TISSUE OXYGENATION

Unlike hypoxemia which denotes a low PaO_2 and has standard normal and abnormal values, there are no normal values for tissue PO_2 and it cannot be routinely measured at the bedside. Tissue hypoxia is defined as abnormal O_2 utilization by cells and should be distinguished from other terms, such as hypoxic, anemic, histotoxic, and stagnant hypoxia, which can lead to but are not synonymous with tissue hypoxia. There are three ways to detect tissue hypoxia.

Clinical Assessment

Clinical examination should be the first step in assessing tissue oxygenation. A number of well-known signs (mental obtundation, oliguria, abnormal vital signs, delayed capillary refill) often indicate specific organ dysfunction as a sequel of tissue hypoxia. However, clinical signs are often insensitive as they occur late during the course of tissue hypoxia. Direct or indirect measurements of local tissue oxygenation of an organ suspected to suffer from hypoxia will facilitate the assessment. Local tissue oxygen probes have been used in critical care areas in some instances (e.g., brain).

■ Physiological Parameters

Mixed Venous O₂ Saturation (SvO₂)

Mixed venous blood represents blood returning from all the venous beds of the body, "mixed" together in the right ventricle. It is obtained from the distal end of the pulmonary artery with the help of a specialized pulmonary artery catheter, the tip of which emits infrared light and records light reflected back from Hb in circulating erythrocytes. This technique is called reflectance spectrophotometry (whereas pulse oximeters use transmission spectrophotometry). SvO₂ can also be measured intermittently by withdrawing blood from the catheter. In the proximal part of the pulmonary artery, blood from the two vena cavae and coronary sinus is not fully blended and therefore does not represent total body venous gas values. SvO2 is a marker of the balance between whole body DO₂ and O₂ demand and is normally between 65 and 75%; that is, O_2 demand is usually about 25–35% that of O₂ delivery.

Causes of Decreased SvO₂

- Decrease in $\dot{D}O_2$: This may occur due to hypovolemia, decreased cardiac output, low Hb, low PaO₂ and SaO₂.
- Increase in O₂ demand: Critical illness, sepsis, thyrotoxicosis, etc.

Causes of Increased SvO₂

- *Increased DO*₂: Increased cardiac output (e.g., exercise, use of inotropes), increased Hb (hypertransfusion).
- Decrease in O₂ demand: Deep sedation and paralysis in ventilated patients.
- Decreased tissue O₂ utilization: Cyanide and CO poisoning, sepsis.
- Left-to-right shunts: These can usually be diagnosed by an abnormal "step-up" of SvO₂ at the level of the defect as the pulmonary artery catheter is passed into the right atrium or ventricle.

A limitation of SvO_2 as a parameter for assessing tissue oxygenation is that normal or increased values do not always mean that tissue oxygenation is adequate. For example, in sepsis and CO poisoning, impaired tissue O_2 utilization results in a normal or high SvO_2 . In addition, pathologic vasodilatation and increased cardiac output in sepsis also tend to increase SvO_2 even though tissue hypoxia is ongoing.

Dual Oximetry

By simultaneously measuring SaO_2 by pulse oximetry, one can get a continuous measurement of whole-body O_2 extraction, i.e., SaO_2 – SvO_2 . This method is known as dual oximetry and its normal value is 20–30%.

DO₂/VO₂ Measurements

The measurement of changes in $\dot{V}O_2$ in response to changes in $\dot{D}O_2$ has been suggested as a sensitive method of determining whether tissue hypoxia exists. However, it entails multiple measurements at baseline and after various interventions carried out to increase $\dot{D}O_2$ (such as the administration of fluids and inotropes) and is therefore impractical.

Blood Lactate Level

Blood lactate levels increase when tissue hypoperfusion results in anaerobic metabolism. This is known as type A lactic acidosis and is different from type B or nonhypoxic causes of lactic acidosis, e.g., delayed clearance of lactate due to liver disease, thiamine deficiency (blocks pyruvate metabolism), and metabolic alkalosis (stimulates glycolysis). A blood lactate value >4 mmol/L is generally taken as abnormal. It is easy to measure and can be followed sequentially to assess prognosis as well as response to therapy. Recent studies indicate that blood lactate concentrations are a better prognostic indicator than oxygen-derived physiological variables.

Gastric Tonometry

Physiological variables of oxygen transport detailed above and lactate are the indices of global tissue oxygenation and cannot identify oxygen deficits in individual organs. This leads to the development of gastric tonometry to measure regional perfusion in the gut that employs a balloon in the stomach to measure intramucosal pH (pHi). Despite its complexity, tonometry is a reasonably good prognostic indicator in critically ill patients.

Sublingual Capnography

Recently capnography in the sublingual area, a technique that is less invasive and easier to use, has been shown to yield tissue PCO₂ measurements that correlate with those obtained by gastric tonometry.

Nuclear Magnetic Resonance Spectrometry

This laboratory technique, not applicable at the bedside, can measure biochemical processes at the cellular level, e.g., levels of ATP, NADH, and cytochrome oxidase. Radionuclide imaging, such as positron emission tomography (PET) scanning, has emerged as an important tool to characterize tumor oxygenation to optimize and individualize therapy for cancers.

Most of the different parameters of in vivo oxygen measurements measure different things and differ in their sensitivity, accuracy, and repeatability. It has been proposed that a proper model that relates the various measurements to each other can serve as a powerful tool to assess tissue oxygenation. Unfortunately, such a functional model is not available as yet, whereas the measurement of SvO_2 requires the placement of a pulmonary arterial catheter.

SUMMARY

Tissue oxygenation involves the amount of oxygen delivered and subsequently consumed by the tissues for its metabolic needs. While delivery of oxygen depends upon the arterial oxygen content and cardiac output, its consumption by the tissues is more complex, varies for different organ tissues depending upon the normality of function. Failure to maintain oxygenation results in tissue hypoxia, cellular malfunction and death. Adequate of tissue oxygenation is assessed with measurements of both clinical and physiological parameters which have been discussed earlier in the chapter.

SUGGESTED READINGS

- Dantzker DR, Macintyre NR, Bakow ED. Comprehensive Respiratory Care. Philadelphia: W.B. Saunders Company; 1995.
- Dickens JJ. Central venous oxygenation saturation monitoring: A role for critical care? Curr Anaesth Crit Care. 2004;15: 378-82.
- 3. Dunn J-OC, Mythen MG, Grocott MP. Physiology of oxygen transport. BJA Educ. 2016;16:341-8.
- Hollenberg SM, Ahrens TS, Annane D, et al. Practice parameters for hemodynamic support of sepsis in adult patients: 2004 update. Crit Care Med. 2004; 32(9):1928-48.
- Krause BJ, Beck R, Souvatzoglou M, et al. PET and PET/CT studies of tumor tissue oxygenation. Q J Nucl Med Mol Imaging. 2006;50(1):28-43.
- Leach RM, Treacher DF. The pulmonary physician in critical care * 2: oxygen delivery and consumption in the critically ill. Thorax. 2002;57(2):170-7.
- 7. Lumb AB. Nunn's Applied Respiratory Physiology, 8th edition, Edinburgh: Elsevier; 2017.

- 8. Malley WJ (Ed). Oxygen transport and internal respiration. In: Clinical Blood Gases, 1st edition. Philadelphia: WB Saunders Company; 1990. pp. 85-101.
- Marino P (Ed). Tissue oxygenation. In: The ICU Book, 2nd edition. Philadelphia: Lippincott Williams and Wilkins; 1998. pp. 187-203.
- 10. Nathan AT, Singer M. The oxygen trail: tissue oxygenation. Br Med Bull. 1999;55(1):96-108.
- Reinhart K, Kuhn HJ, Hartog C, et al. Continuous central venous and pulmonary artery oxygen saturation monitoring in the critically ill. Intensive Care Med. 2004;30(8):1572-8.
- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-77.
- Swartz HM, Dunn J. The difficulties in comparing in vivo oxygen measurements: turning the problems into virtues. Adv Exp Med Biol. 2005;566:295-301.
- 14. John B. West JB. Respiratory Physiology: The Essentials, 9th edition. Philadelphia: Wolters Kluwer; 2012.

Textbook of Pulmonary & Critical Care Medicine

The third edition of the two-volume *Textbook of Pulmonary & Critical Care Medicine* provides most recent information and reference material for postgraduate students and teachers of pulmonary sciences, general medicine, thoracic surgeons, pediatrics, critical care, and other clinical specialties. It is equally useful for medical practitioners of different specialties, especially those handling patients with lung involvement. The authorship list includes about 300 eminent pulmonologists and critical care specialists not only from India, but also from several different countries. It specifically focuses on epidemiology, pathophysiology, pulmonary interventions, newer diagnostic techniques, and treatment modalities of different respiratory disorders. Besides the sections on respiratory physiology, diagnosis modalities and different lung diseases, there are also chapters on pulmonary perspectives such as history, ethics, and health economics. There is comprehensive coverage of up-to-date information on pulmonary critical care and sleep medicine. A large number of tables, figures, and algorithms make it highly attractive and reader-friendly for an easy understanding.

Surinder K Jindal MD FAMS FNCCP FICS FCCP is a Professor Emeritus and former Head of Pulmonary Medicine of the premier Postgraduate Institute of Medical Education and Research in India, is a man with an extensive experience of over 45 years. He has occupied several academic, administrative, and research positions during his career. Besides extensively writing scientific papers, chapters, and books on various issues, he has also served on Editorial Boards of different professional journals. He was the first in the country to introduce the Postdoctoral Fellowship Program in India in 1989 and mentored a whole lot of pulmonologists spread all over India and abroad. He has been bestowed with several different honors which include Lifetime Achievement Awards of Indian Societies as well as the Outstanding International Educator Award of the American Thoracic Society.

Printed in India



Available at all medical bookstores or buy online at www.ejaypee.com



JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Darvagani, New Delbi - 110 002, INDIA

EMCA House, 23/23-B, Ansari Road, Daryaganj, New Delhi - 110 002, INDIA www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers Follow us on instagram.com/JaypeeMedicalPublishers

Shelving Recommendation **MEDICINE**

