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Beth A. Pletcher and Nelson L. Turcios

Congenital bronchopulmonary malformations are relatively common and arise during various periods of morphogenesis. Although some are isolated or sporadic occurrences, others may result from single gene mutations or cytogenetic imbalances. Single gene mutations have been identified, which are etiologically related to primary pulmonary hypoplasia, lung segmentation defects as well as pulmonary vascular and lymphatic lesions. Functional defects in cystic fibrosis, primary ciliary dyskinesias, alpha-1-antitrypsin deficiency, and surfactant proteins caused by gene mutations may result in progressive pulmonary disease. This article provides an overview of pediatric pulmonary disease from a genetic perspective.

Pulmonary Manifestations of Congenital Heart Disease in Children	25
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Brandy N. Johnson, Julie L. Fierro, and Howard B. Panitch

This review addresses how anomalous cardiovascular anatomy imparts consequences to the airway, respiratory system mechanics, pulmonary vascular system, and lymphatic system. Abnormal formation or enlargement of great vessels can compress airways and cause large and small airway obstructions. Alterations in pulmonary blood flow associated with congenital heart disease (CHD) can cause abnormalities in pulmonary mechanics and limitation of exercise. CHD can lead to pulmonary arterial hypertension. Lymphatic abnormalities associated with CHD can cause pulmonary edema, chylothorax, or plastic bronchitis. Understanding how the cardiovascular system has an impact on pulmonary growth and function can help determine options and timing of intervention.

Pulmonary Manifestations of Gastrointestinal, Pancreatic, and Liver Diseases in Children	41
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Emily R. Le Fevre, Kathleen H. McGrath, and Dominic A. Fitzgerald

Pulmonary manifestations of gastrointestinal (GI) diseases are often subtle, and underlying disease may precede overt symptoms. A high index of suspicion and a low threshold for consultation with a pediatric pulmonologist is warranted in common GI conditions. This article outlines the pulmonary manifestations of different GI, pancreatic, and liver diseases

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in children, including gastroesophageal reflux disease, inflammatory bowel disease, pancreatitis, alpha1-antitrypsin deficiency, nonalcoholic fatty liver disease, and complications of chronic liver disease (hepatopulmonary syndrome and portopulmonary hypertension).

Pulmonary Manifestations of Hematologic and Oncologic Diseases in Children

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Lama Elbahlawan, Antonio Moreno Galdo, and Raul C. Ribeiro

Pulmonary complications are common in children with hematologic or oncologic diseases, and many experience long-term effects even after the primary disease has been cured. This article reviews pulmonary complications in children with cancer, after hematopoietic stem cell transplant, and caused by sickle cell disease and discusses their management.

Pulmonary Manifestations of Endocrine and Metabolic Diseases in Children

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Alexander A. Broomfield, Raja Padidela, and Stuart Wilkinson

Advances in technology, methodology, and deep phenotyping are increasingly driving the understanding of the pathologic basis of disease. Improvements in patient identification and treatment are impacting survival. This is true in endocrinology and inborn errors of metabolism, where disease-modifying therapies are developing. Inherent to this evolution is the increasing awareness of the respiratory manifestations of these rare diseases. This review updates clinicians, stratifying diseases spirometrically; pulmonary hypertension and diseases with a predisposition to recurrent pulmonary infection are discussed. This division is artificial; many diseases have multiple pathologic effects on respiration. This review does not cover the impact of obesity.

Pulmonary Manifestations of Immunodeficiency and Immunosuppressive Diseases Other than Human Immunodeficiency Virus

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Susan E. Pacheco and James M. Stark

Immune deficiencies may alter normal lung function and protective mechanisms, resulting in a myriad of pulmonary manifestations. Primary immunodeficiencies involve multiple branches of the immune system, and defects may predispose to recurrent upper and lower respiratory infections by common pathogens; opportunistic infections; and autoimmune, inflammatory, and malignant processes that may result in interstitial pneumonias. Secondary immunodeficiencies may result from neoplasms or their treatment, organ transplant and immunosuppression, and from autoimmune diseases and their treatments. Primary and secondary immunodeficiencies and their pulmonary manifestations may be difficult to diagnose and treat. A multidisciplinary approach to evaluation is essential.

Respiratory Complications in Children and Adolescents with Human Immunodeficiency Virus

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Leah Githinji and Heather J. Zar

Respiratory complications comprise a large proportion of the burden of mortality and morbidity in children with human immunodeficiency virus (HIV). HIV-associated lower respiratory tract infection (LRTI) has declined

in incidence with early diagnosis and use of antiretroviral therapy (ART) but is widespread in areas with limited access to ART. HIV-exposed uninfected infants have a higher risk of LRTI early in life than unexposed infants. Pulmonary tuberculosis (PTB) presenting as acute or chronic disease is common in highly TB endemic areas. Chronic lung disease is common; preceding LRTI, PTB or late initiation of ART are risk factors.

Pulmonary Manifestations of Rheumatic Diseases in Children

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Mary M. Buckley and C. Eglar Rabinovich

Children with rheumatic disease have rare pulmonary manifestations that may cause significant morbidity and mortality. These children are often clinically asymptomatic until disease has significantly progressed, so they should be screened for pulmonary involvement. There has been recent recognition of a high mortality-related lung disease in systemic-onset juvenile idiopathic arthritis; risk factors include onset of juvenile idiopathic arthritis less than 2 years of age, history of macrophage activation syndrome, presence of trisomy 21, and history of anaphylactic reaction to biologic therapy. Early recognition and treatment of lung disease in children with rheumatic diseases may improve outcomes.

Pulmonary Manifestations of Systemic Vasculitis in Children

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Muserref Kasap Cuceoglu and Seza Ozen

Vasculitides are defined according to the vessel size involved, and they tend to affect certain organ systems. Pulmonary involvement is rare in the common childhood vasculitides, such as Kawasaki disease, IgA vasculitis (Henoch Schonlein purpura). On the other hand, lung involvement is common in a rare pediatric vasculitis, granulomatosis with polyangiitis (GPA) (Wegener granulomatosis), where respiratory system findings are common. A criterion in the Ankara 2008 classification criteria for GPA is the presence of nodules, cavities, or fixed infiltrates. The adult data suggest that rituximab may be an alternative to cyclophosphamide in induction treatment.

Respiratory Complications of Pediatric Neuromuscular Diseases

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John R. Bach, Nelson L. Turcios, and Liping Wang

Respiration is an event of oxygen consumption and carbon dioxide production. Respiratory failure is common in pediatric neuromuscular diseases and the main cause of morbidity and mortality. It is a consequence of lung failure, ventilatory pump failure, or their combination. Lung failure often is due to chronic aspiration either from above or from below. It may lead to end-stage lung disease. Ventilatory pump failure is caused by increased respiratory load and progressive respiratory muscles weakness. This article reviews the normal function of the respiratory pump, general pathophysiology issues, abnormalities in the more common neuromuscular conditions and noninvasive interventions.

Pulmonary Manifestations of Parasitic Diseases in Children

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Teena Huan Xu, Nair Lovaton, Jose Serpa, and Theresa J. Ochoa

Parasites can cause respiratory symptoms through focal or diffuse lung involvement, depending on the location of the parasite and the host's immune response. Pulmonary involvement can be a major feature of some parasitic infections or a complication during transpulmonary larval migration. Parasites should be included in the differential diagnosis of common lung diseases, especially in the presence of peripheral eosinophilia or extrapulmonary symptoms (abdominal pain, diarrhea, jaundice, skin lesions).

Pulmonary Manifestations of Renal Disorders in Children

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Laura Malaga-Diequez, Howard Trachtman, and Robert Giusti

The causes of kidney disease in pediatric patients are evenly divided between congenital abnormalities of the kidney and urinary tract and acquired disorders. Nearly 10% to 15% of adults in the United States have chronic kidney disease (CKD); there are no comparable data in children. Regardless of patient age, CKD is a systemic problem that affects every organ system, including the lung. We review the tests used to diagnose and evaluate kidney disease and the main clinical syndromes that are likely to be encountered to aid the pulmonology consultant who is asked to evaluate patients with kidney disease.

Functional Respiratory Disorders in Children

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Manju Hurvitz and Miles Weinberger

Functional respiratory disorders (FRDs) are those characterized by respiratory symptoms without anatomic or organic etiology. Clinicians caring for children encounter these disorders and should be familiar with diagnosis and treatment. FRDs encompass the habit cough syndrome and its variants, vocal cord dysfunction, hyperventilation disorders, functional dyspnea, and sighing syndrome. Failure to identify these disorders results in unnecessary testing and medication. This article reviews the clinical presentation, manifestation, and treatment of respiratory FRDs in children. How health care providers can successfully identify and treat these reversible conditions in the clinical setting is discussed.

Pulmonary Implications of Pediatric Spinal Deformities

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Diane Dudas Sheehan and John Grayhack

Pediatric spinal deformities may be associated with pulmonary complications in a patient's lifetime. A review of the diagnosis of spinal abnormalities includes classifications of scoliosis and kyphosis, correlating physical examination findings and radiographic interpretation. The natural history of untreated spine deformities is reviewed along with the associated altered pulmonary compromise. Treatment options for children affected by spinal deformities are discussed, including the relative indications, the efficacy, pros and cons of different treatment options, along with the evidence to support these. This overview of spine deformities includes research outcomes to support the care of these pediatric patients.

Pulmonary Manifestations of Skin Disorders in Children 261

Bernard A. Cohen and Nelson L. Turcios

Systemic diseases often manifest with cutaneous findings. Many pediatric conditions with prominent skin findings also have significant pulmonary manifestations. These conditions include both inherited multisystem genetic disorders such as yellow-nail syndrome, neurofibromatosis type 1, tuberous sclerosis complex, hereditary hemorrhagic telangiectasia, Klippel-Trénaunay-Weber syndrome, cutis laxa, Ehlers-Danlos syndrome, dyskeratosis congenita, reactive processes such as mastocytosis, and aquagenic wrinkling of the palms. This overview discusses the pulmonary manifestations of skin disorders.

Adverse Environmental Exposure and Respiratory Health in Children 277

Peter D. Sly

The burden imposed by pollution falls more on those living in low-income and middle-income countries, affecting children more than adults. Most air pollution results from incomplete combustion and contains a mixture of particulate matter and gases. Air pollution exposure has negative impacts on respiratory health. This article concentrates on air pollution in 2 settings, the child's home and the ambient environment. There is an inextricable 2-way link between air pollution and climate change, and the effects of climate change on childhood respiratory health also are discussed.

Inequalities and Inequities in Pediatric Respiratory Diseases 293

Paulo Camargos and Kimberly Danieli Watts

Social inequality refers to disparities in society that have the effect of limiting a group's socioeconomic, educational, and intellectual potential. Inequity in health means any limitation to access comprehensive health services that also hinders the achievement of well-being and favorable health outcomes. Strategies for more equitable growth to eradicate global poverty would contribute to reducing health inequities and improve health care outcomes. Coordinated efforts between governments, private sector, families, and interested stakeholders are needed. This article discusses inequality and inequity in pediatric respiratory diseases, the challenges confronted, and the strategies needed to mitigate these disparities.

High-altitude Illnesses and Air Travel: Pediatric Considerations 305

Nelson Villca, Adriana Asturizaga, Alexandra Heath-Freudenthal

Healthy children may present acute mountain sickness (AMS) within a few hours after arrival at high altitudes. In few cases, serious complications may occur, including high-altitude pulmonary edema and rarely high-altitude cerebral edema. Those with preexisting conditions especially involving hypoxia and pulmonary hypertension shall not risk travelling to high altitudes. Newborn from low altitude mothers may have prolonged time to complete postnatal adaptation. The number of children and adolescents traveling on commercial aircrafts is growing, and this poses a need for their treating physicians to be aware of the potential risks of hypoxia while air traveling.

Risk Factors for Severity in Children with Coronavirus Disease 2019: A Comprehensive Literature Review

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Sophia Tsabouri, Alexandros Makis, Chrysoula Kosmeri, and Ekaterini Siomou

The coronavirus disease 2019 (COVID-19) pandemic has affected hundreds of thousands of people. The authors performed a comprehensive literature review to identify the underlying mechanisms and risk factors for severe COVID-19 in children. Children have accounted for 1.7% to 2% of the diagnosed cases of COVID-19. They often have milder disease than adults, and child deaths have been rare. The documented risk factors for severe disease in children are young age and underlying comorbidities. It is unclear whether male gender and certain laboratory and imaging findings are also risk factors. Reports on other potential factors have not been published.