Pulmonary Medicine: At the Forefront of Clinical Medicine, Advanced Technology, and Innovative Research

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Pulmonary medicine, a major subspecialty of internal medicine, has advanced dramatically over the past decade and continues to grow at an impressive pace. The subspeciality is a uniquely multifaceted field, requiring thoughtful integration of the patient's history, physical findings, laboratory data, and imaging to reach an accurate diagnosis and suggest proper treatment. This clinical depth is complemented by a rapidly expanding therapeutic arsenal for complex lung diseases. At the same time, technological progress has transformed our practice. Innovations in imaging and in both diagnostic and therapeutic bronchoscopy–central components of interventional pulmonology–have evolved so rapidly that tools used only a decade or two ago now seem outdated [1]. All these advancements offer meaningful opportunities to enhance the health outcomes of our patients. What a fascinating specialty and what an exciting time to be a pulmonologist.

Pulmonary medicine encompasses diverse conditions arising from the various compartments of the respiratory system and the anatomy and physiology of the lungs. Airway diseases such as chronic obstructive pulmonary disease (COPD), asthma, and bronchiectasis remain a cornerstone of lung diseases and pulmonary practice. Interstitial lung diseases involve the structural framework of the lung, while pulmonary vascular diseases center on the pulmonary circulation. As a primary gateway to the external environment, the lungs are also a common site for both common and rare infections.

This special issue of the *Israel Medical Association Journal* (*IMAJ*) offers a diverse collection of original research, as well as a review, highlighting work of substantial clinical and academic relevance produced by our colleagues in the field. These contributions illustrate the multidimensional nature of pulmonary clinical medicine and research and the evolving challenges and opportunities shaping our specialty.

COPD and other smoking-related diseases remain a significant and continuous burden on public health and on pulmonary practice, particularly among the elderly. An ongoing debate persists regarding the optimal diagnostic criteria for COPD, especially given the challenge of distinguishing normal aging from true disease [2]. Berg and colleagues [3] addressed the potential pitfalls and risk of overdiagnosis when defining obstruction in older adults using the traditional forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) ratio < 0.7. The authors compared this conventional cutoff with an individualized lower limit of normal approach.

The association between COPD and cardiovascular system complications, including increased mortality, has become a central topic in current pulmonary research. A growing body of evidence highlights the link between COPD exacerbations and heightened cardiovascular risk [4]. Kassirer et al. [5] explored a new potential predictor of cardiovascular events following the first episode of COPD exacerbation and identified the neutrophil-to-lymphocyte ratio as a promising biomarker. Epshtein et al. [6] further examined the boundaries between normal physiology and disease in older adults, aiming to define the normal reference ranges for arterial blood gases (O_2 and CO_2) in the elderly population.

The global and Israeli shortage of organs for transplant continues to limit our ability to treat the most severely ill pulmonary patients [7]. Individuals awaiting lung transplantation require meticulous and compassionate care and monitoring, as they truly represent the frontier of pulmonary medicine capabilities. Research in this population carries important clinical implications. To better stratify risks in patients waiting for transplantation, Izhakian and co-authors [8], reported on sex-based disparities

in mortality among COPD patients on the lung-transplant waiting list. In their study, female sex was identified as a major risk factor for increased mortality. At the other end of the life spectrum, Jacobi and colleagues [9] shared their experience with pediatric lung transplantation, summarizing outcomes in 29 children with severe lung diseases, with a median age of 14 years.

The early diagnosis and staging of lung cancer continue to pose major challenges in pulmonary medicine. These efforts advance in parallel with developments in bronchoscopic techniques and laboratory methods [10]. Abdel-Rahman and colleagues [11] from Shaare Zedek Medical Center presented a retrospective analysis of their experience collecting cytological samples for next-generation sequencing (NGS) in patients with non-small cell lung cancer, highlighting both current practices and anticipated future advancements.

Interstitial lung diseases have gained significant attention over the past decade, largely due to the emergence of effective new therapies. Sarcoidosis, a distinctive multisystem disease with predominant pulmonary involvement, varies markedly across countries and ethnic groups, necessitating region-specific characterization [12]. Mor et al. [13] described the epidemiology and different clinical features of sarcoidosis across diverse ethnic populations in Israel, emphasizing unique patterns in comparison with global data and notable differences between Jewish and Arab patients.

The coronavirus disease 2019 (COVID-19) pandemic placed pulmonary physicians at the forefront of care for this widespread and devastating disease. Over the course of 3 years, pulmonologists diagnosed and treated thousands of patients, saving innumerable lives. Alongside clinical care, several important research contributions emerged from our community [14]. Such is the work by Wand et al. [15], that identified an association between the RT-PCR cycle threshold at diagnosis and clinical outcomes among hospitalized COVID-19 patients. Continued attention to pulmonary infections and occupational exposures is also reflected in the case series reported by Izhakian and co-authors [16] who described an intriguing link between artificial stone related silicosis, a condition extensively studied in Israel, and non-tuberculous mycobacterial infections.

As the field of invasive pulmonology continues to advance, particularly with increasingly sophisticated bronchoscopic technologies and more [1], the need to recognize and manage procedure-related complications grows. Our colleagues remained dedicated to identifying modern strategies to prevent and treat such events. In their review, Heching et al. [17] described the use of hyperbaric oxygen therapy for a rare yet dangerous complication of transbronchial lung biopsy: cerebral arterial air embolism. Maintaining a high index of suspicion for this uncommon but potentially fatal complication is essential for timely diagnosis and prompt treatment.

This collection of articles, which comprises this special issue of *IMAJ*, reflects the Israeli pulmonology community's commitment to clinical and research excellence and underscores the complexity and distinctive appeal of this rapidly evolving specialty.

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The past is never where you think you left it.

Katherine Anne Porter (1890–1980), American journalist, essayist, short story writer, novelist, poet and political activist

Capsule

Noninferiority of one HPV vaccine dose to two doses

In this trial, **Kreimer** and colleagues assessed whether one dose of an HPV vaccine was noninferior to two doses. Girls 12 to 16 years of age were randomly assigned, in a 1:1:1:1 ratio, to receive one or two doses of a bivalent HPV vaccine or one or two doses of a nonavalent HPV vaccine. The primary end point was new HPV type 16 or 18 infection occurring from month 12 to month 60 and persisting for at least 6 months. The prespecified noninferiority margin was 1.25 infections per 100 participants. The authors also assessed vaccine effectiveness by comparing HPV16 or HPV18 infection among the trial participants with that among girls and women enrolled in a nonrandomized survey. A total of 20,330 participants were enrolled and underwent randomization, and 3005 unvaccinated participants were enrolled in the survey. The noninferiority analysis showed that one vaccine dose was noninferior to two doses in preventing HPV16 or HPV18 infection. The rate difference between one and two doses of the bivalent vaccine was −0.13 infections per 100 participants (95% confidence interval [95%CI] −0.45 to 0.15; $P < 0.001$ for noninferiority), and the difference between one and two doses of the nonavalent vaccine was 0.21 infections per 100 participants (95%CI, −0.09 to 0.51; $P < 0.001$ for noninferiority). The vaccine effectiveness was at least 97% in each of the four trial groups. No safety concerns were identified.

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Capsule

Updated evidence for COVID-19, RSV, and influenza vaccines for 2025–2026

Scott et al. conducted a systematic review of U.S.-licensed immunizations against coronavirus disease 2019 (COVID-19), respiratory syncytial virus (RSV), and influenza. Of 17,263 identified references, 511 met the inclusion criteria. COVID-19 mRNA vaccines against the XBB.1.5 subvariant had pooled vaccine effectiveness against hospitalization of 46% (95% confidence interval [95%CI] 34–55; from cohort studies) and 50% (95%CI 43–57; from case-control studies) among adults and 37% (95%CI 29–44) among immunocompromised adults. In a case-control study, vaccines against the KP.2 subvariant showed an effectiveness of 68% (95%CI 42–82). Maternal RSV vaccination (for infant protection), nirsevimab for infants, and RSV vaccines in adults who were 60 years of age or older showed vaccine effectiveness of 68% or more against hospitalization. Influenza vaccination had a pooled vaccine effectiveness of 48% (95%CI 39–55) in adults between the ages of 18 and 64 years and 67% (95%CI 58–75) in children against hospitalization. Safety profiles were consistent with previous evaluations. The diagnosis of myocarditis associated with COVID-19 vaccines occurred at rates of 1.3 to 3.1 per 100,000 doses in male adolescents, with lower risk associated with longer dosing intervals. The RSVpreF vaccine was associated with 18.2 excess cases of Guillain–Barré syndrome per million doses in older adults; a significant association with preterm birth was not observed when the vaccine was administered at 32 to 36 weeks' gestation.

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