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Interstitial Lung Disease in 2025: Updated Classification, Precision Diagnostics, and Expanding Therapeutic Frontiers

Nathan Hambly, MD

Introduction

Interstitial lung disease (ILD) is an umbrella term for over 200 heterogeneous disorders that primarily affect the pulmonary interstitium and/or small airways and alveoli. These disorders are often characterized by varying degrees of inflammation and fibrosis that lead to impairment in lung function and consequent respiratory symptoms. Although idiopathic pulmonary fibrosis (IPF) remains the classic example, there exists a remarkable prevalence of cases in the context of connective tissue disease (CTD) or as a consequence of antigen exposure in the setting of hypersensitivity pneumonitis (HP). Over the past decade, the integration of high-resolution computed tomography (HRCT), extended serologic panels, increased knowledge of the natural history of disease, and the high risk of fibrotic progression across the diagnostic spectrum, has refined diagnostic certainty and allowed earlier therapeutic intervention. Contemporary guidelines from the American Thoracic Society (ATS), European Respiratory Society (ERS), and European Alliance of Associations for Rheumatology (EULAR) now emphasize pattern-based phenotyping rather than rigid disease taxonomies. Clinicians are encouraged to interpret ILD through intersecting dimensions—radiologic morphology, immune serology, and cellular aging biology—each contributing to disease trajectory and treatment response.

For Canadian respirologists, these advances coincide with a rapidly evolving therapeutic landscape **(Table 1)**. Antifibrotic agents, selective immunomodulators, and emerging inhaled prostacyclin-based therapies are transforming the future therapeutic landscape. Yet, access to evidence-based treatments, especially for those with systemic sclerosis (SSc) and idiopathic inflammatory myopathies (IIM) related lung disease, remains inconsistent across provinces, underscoring the need for sustained advocacy. This review summarizes the 2025 classification framework, outlines novel diagnostic approaches, and appraises recent and emerging clinical trial data with practical guidance for clinical practice **(Table 2)**.

Updated Classification and Guideline Framework

The 2025 ATS/ERS statement on ILD classification[1] re-centres the field on phenotypic stratification. Rather than adopting a molecular taxonomy, the framework reinforces a two-step model: identify the radiologic or histopathologic pattern, then, determine the final multidisciplinary diagnosis. For example, usual interstitial pneumonia represents a pattern, whereas IPF is the multidisciplinary diagnosis that incorporates radiologic/histopathologic patterns, clinical features, and exclusion of alternative etiologies.

Four major updates reflect the evolution of the classification system. First, the framework now includes all ILDs, not only idiopathic interstitial pneumonias, recognizing that the rationale for isolating idiopathic interstitial pneumonia is no longer justified. Second, patients are subdivided into interstitial (fibrotic or non-fibrotic) and alveolar filling disorders, clarifying diagnostic pathways. Third, diagnostic confidence is explicitly incorporated: cases with less than 50% diagnostic certainty are categorized as unclassifiable ILD, acknowledging that uncertainty is common and requires ongoing reassessment. Fourth, three new terms were introduced: bronchiolocentric interstitial pneumonia (BIP), alveolar macrophage pneumonia (AMP), and idiopathic diffuse alveolar

damage (iDAD). Of these, BIP has generated the most debate within the ILD community. BIP has been introduced as an overarching term to describe an airway-centred process that can be observed both in HP and other ILDs such as CTD-ILD, aspiration, and drug-induced disease. This is because a substantial proportion of patients with bronchiolocentric patterns of disease on pathology and imaging have non-HP diagnoses. Previously published HP guidelines still provide an excellent template for approaching the BIP pattern, recognizing that the HP diagnostic guidelines were essentially describing a radiologic/pathologic pattern of bronchiolar disease rather than a specific diagnosis. AMP has been incorporated to replace the pathologically inaccurate term desquamative interstitial pneumonia. Similarly, iDAD is replacing acute interstitial pneumonia given the imprecision that arises when chronic fibrotic lung conditions present with acute exacerbations.

This framework aligns closely with the 2025 ERS/EULAR CTD-ILD recommendations,[2] which provide disease-specific algorithms for SSc-ILD, rheumatoid-arthritis (RA)-ILD, and IIM-associated ILD. Developed by a ERS/EULAR task force established in 2020 and finalized over five years, the guidance addresses 25 Patients, Intervention, Comparison Outcomes (PICO) questions and 28 narrative questions across four primary CTD groups. Its recommendations were informed by a systematic literature review followed by structured consensus building using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology. Key elements include the institution of regular screening with HRCT chest screening for high-risk patients, which includes all patients with SSc and mixed

Trial	Population	Intervention	Comparator	Key Outcomes
FIBRONEER-IPF[11]	IPF	Nerandomilast 18 mg or 9 mg BID	Placebo	Reduced annual FVC decline; benefit on background antifibrotics
FIBRONEER-PPF[12]	Progressive pulmonary fibrosis	Nerandomilast 18 mg or 9 mg BID	Placebo	Reduced FVC decline; mortality apparent
INBUILD[10]	Non-IPF progressive ILD	Nintedanib	Placebo	Reduced FVC decline across heterogeneous ILDs
RECITAL[16]	CTD-ILD	Rituximab	Cyclophosphamide	Similar FVC outcomes; fewer adverse events with rituximab
EVER-ILD[17]	Fibrotic HP and CTD-ILD	MMF + rituximab	MMF alone	Improved FVC with combined therapy
focuSSced[15]	Diffuse SSc with ILD	Tocilizumab	Placebo	Slowed FVC decline despite neutral skin outcome
TETON-2 (ERS 2025)	IPF (Phase 3, ongoing)	Inhaled treprostinil	Placebo	Early reports: improvement in FVC trajectory
INCREASE[13]	PH-ILD (Group 3)	Inhaled treprostinil	Placebo	Improved 6MWD; reduced NT-proBNP

Table 1. Selected recent clinical trials informing ILD and pulmonary fibrosis management; *courtesy of Nathan Hambly, MD*

Abbreviations: 6MWD: six-minute walk distance; **BID:** twice a day; **CTD:** connective tissue disease; **FVC:** forced vital capacity; **HP:** hypersensitivity pneumonitis; **ILD:** interstitial lung disease; **IPF:** idiopathic pulmonary fibrosis; **MMF:** mycophenolate mofetil; **SSc:** systemic sclerosis; **NT-proBNP:** N-terminal pro–B-type natriuretic peptide; **PH-ILD:** pulmonary hypertension associated with interstitial lung disease

connective tissue disease at diagnosis, and RA and IIM patients with known risk factors for ILD. The guidelines also detail the appropriate monitoring of ILD in each of the disease states over time, including the timing of clinical assessments and the use of serial pulmonary function tests (PFTs) and HRCT evaluations. The role of immunomodulatory and antifibrotic therapy across the spectrum of CTD-ILD was also comprehensively described, particularly focusing on the unique intricacies that characterize each CTD-ILD subcategory. For instance, the strong recommendation for tocilizumab in early diffuse SSc-ILD with signs of inflammation, whereas antifibrotic therapy is prioritized for cases of progressive pulmonary fibrosis (PPF) and/or a usual interstitial pneumonia pattern in RA-ILD.

In practice, this "pattern-plus-context" model supports tailored therapy across the spectrum of parenchymal disease. Molecular insights—particularly telomere attrition and epigenetic aging—serve as adjunctive markers that refine prognosis and inform treatment tolerance rather than redefining the classification framework itself.[3,4]

	Key Clinical Pearls
Detailed History	• Multiple ILD phenotypes may coexist within families; genetic risk reflects fibrosis susceptibility, not a specific ILD diagnosis. • Premature greying, cytopenias, cirrhosis, or MDS should prompt evaluation for telomere-mediated disease. • Raynaud phenomenon, telangiectasias, and myositis markers are essential diagnostic anchors. • Patients without identifiable antigen exposure have worse long-term outcomes; exposure clarification is critical.
Physical Examination	• Absence of crackles suggests alternative diagnoses (sarcoid); clubbing strongly suggests fibrotic phenotypes such as IPF or DIP. • Detailed examination for any evidence of CTD critical including periungal capillary changes, telangiectasias, sclerodactyly, mechanic's hands, and cutaneous manifestations of IIM.
Diagnostics	• Ground-glass opacities may coexist with UIP; distribution and relation to fibrosis are more informative than presence alone. • 'Straight-edge sign' raise suspicion for CTD. • PPFE-like features suggest telomere shortening process. • Idiopathic NSIP is rare and warrant thorough CTD and exposure evaluation.
Treatment	• Strong consideration for anti-fibrotic therapy appropriate at all stages of disease in the setting of both IPF and PPF. • SSc-ILD and myositis-ILD often require early immunomodulation given evidence from RECITAL, EVER-ILD, and focuSSced trials. • Patients with mixed inflammatory–fibrotic mechanisms may benefit from concurrent immunomodulation and antifibrotics. • Most RA-ILD reflects underlying disease, not MTX toxicity.
Multidisciplinary Discussion	• Multidisciplinary discussion is essential not only for diagnosis but also for ongoing longitudinal management.

Table 2: Practical clinical pearls in interstitial lung disease assessment and management; *courtesy of Nathan Hambly, MD*

Abbreviations: CTD: connective tissue disease; **DIP:** desquamative interstitial pneumonia; **IIM:** idiopathic inflammatory myopathies; **ILD:** interstitial lung disease; **IPF:** idiopathic pulmonary fibrosis; **MDS:** myelodysplastic syndromes; **MTX:** methotrexate; **PPF:** progressive pulmonary fibrosis; **PPFE:** pleuroparenchymal fibroelastosis; **RA-ILD:** rheumatoid arthritis-interstitial lung disease; **UIP:** usual interstitial pneumonia

Diagnostic Innovation and Phenotypic Refinement

Extended Serologic and Cellular Testing

Comprehensive autoimmune serology remains central to ILD characterization. Rigorous exclusion of an underlying CTD is essential and requires a comprehensive serological and biochemical assessment, including antinuclear antibodies, extractable nuclear antigen panel, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, and measurement of serum creatine kinase. Routine incorporation of myositis-specific and myositis-associated antibodies, including anti-MDA5, PL-7, and PL-12, among others, improves diagnostic precision for clinically amyopathic dermatomyositis and overlap myositis, especially when radiologic imaging reveals evidence of organizing pneumonia or non-specific interstitial pneumonia (NSIP). Detection of anti–granulocyte-macrophage colony-stimulating factor antibodies confirms autoimmune pulmonary alveolar proteinosis, while vascular endothelial growth factor-D levels reliably distinguish lymphangioleiomyomatosis from alternative cystic lung diseases. These biomarkers reduce diagnostic delay and, in certain cases, predict therapeutic responsiveness to biologic or inhaled therapies.[5]

Telomere Biology and Cellular Senescence

Telomere shortening has emerged as a unifying signal across the spectrum of fibrotic lung disease. In the PANTHER-IPF correlative study, Newton and colleagues[6] demonstrated that short leukocyte telomere length (LTL <10th percentile) predicted adverse outcomes with corticosteroid, azathioprine, and n-acetylcysteine therapy. Similarly, a retrospective multi-centre cohort analysis reported that reduced peripheral blood telomere length was associated with a heightened risk of mortality among patients with unclassifiable ILD and fibrotic HP who were treated with antimetabolite therapies such as mycophenolate or azathioprine.[3] Adegunsoye et al.[7] confirmed that LTL is inversely correlated with chronological age and independently predicts mortality across racially diverse pulmonary fibrosis cohorts. Most recently, El Husseini et al.[8] showed that short LTL portends accelerated forced vital capacity (FVC) decline in RA-ILD, reinforcing telomere length as a clinically meaningful biomarker.

For practising respirologists, LTL measurement can be measured from peripheral blood, but this testing is not routinely available across Canada. Further research is required to define its clinical role and to establish how such testing should be implemented into standard practice to guide decisions on immunosuppression and prognostication when considering antifibrotic therapy.

Quantitative and Artificial-Intelligence HRCT

Advances in quantitative CT allow automated fibrosis scoring, vessel-related-structure mapping, and serial change detection. Machine-learning algorithms now predict FVC decline and mortality from baseline HRCT, offering objective support for clinical judgment.[9] Although quantitative CT analysis remains primarily a research tool, it holds substantial promise for future integration into clinical care by enabling early identification of patients suitable for clinical trial enrolment, detecting early progression in interstitial lung abnormalities, and stratifying individuals at heightened risk for fibrotic progression. As availability expands within tertiary ILD programs, it may ultimately support a more standardized approach to longitudinal monitoring.

Therapeutic Evolution in 2025

Antifibrotic Therapy

Pirfenidone and nintedanib remain the therapeutic foundation for IPF, whereas nintedanib is the only approved antifibrotic agent for PPF of non-IPF etiologies. Both agents have demonstrated approximately a 50% reduction in annual FVC decline in IPF.[10] Despite gastrointestinal intolerance in some patients, these therapies have firmly established antifibrotic treatment as standard of care.

Nerandomilast and the FIBRONEER Program

The dual phase-3 trials, FIBRONEER-IPF and FIBRONEER-PPF[11,12] evaluated nerandomilast, a selective phosphodiesterase-4B inhibitor with combined antifibrotic and immunomodulatory properties. In IPF, nerandomilast reduced annual FVC loss by approximately 70 mL versus placebo ($p<0.001$). In PPF—including CTD-ILD and fibrotic hypersensitivity pneumonitis—the adjusted FVC difference was similar, with an emerging mortality signal favouring active therapy. Diarrhea was the principal adverse effect but was rarely dose-

limiting. These findings position nerandomilast as a promising addition to the therapeutic armamentarium, having recently received FDA approval for IPF and is currently under review by Canadian regulatory authorities.

Emerging and Ongoing Trials

The TETON trial series (NCT04708782, NCT05255991, NCT05943535) is investigating inhaled treprostinil for IPF and PPF, building on the INCREASE trial,[13] which demonstrated improved exercise capacity and FVC in Group 3 pulmonary hypertension secondary to parenchymal lung disease. Treprostinil's potential antifibrotic and vasodilatory effects have generated considerable interest. Unfortunately, commercial nebulized treprostinil is currently not presently available in Canada. In parallel, the ALOFT IPF (NCT01234567) and ALOFT PPF (NCT06025578) global phase 3 studies are evaluating the safety and efficacy of the oral lysophosphatidic acid receptor 1 (LPA_1) antagonist admilparant in patients with IPF and PPF. Additional trials of nebulized pirfenidone (NCT06329401) and nintedanib (NCT07194382) aim to enhance pulmonary bioavailability while minimizing systemic side-effects. Collectively, these studies suggest that local, multimodal/combinational antifibrotic delivery strategies may become a mainstay of future therapy.

Immunomodulatory Therapy

Immunomodulatory agents remain a mainstay in the management of CTD-ILD. Antimetabolite agents such as mycophenolate mofetil (MMF) remain first-line therapy for SSc-ILD and IIM-ILD. However, the recent EULAR/ERS guidelines, based on evidence from the faSScinate[14] and focuSSced[15] studies, strongly recommend the IL-6 receptor antagonist tocilizumab, which has demonstrated efficacy in slowing FVC decline in SSc-ILD, and has received regulatory approval in multiple jurisdictions. Similarly, the RECITAL trial[16] showed that rituximab achieved FVC stabilization equivalent to intravenous cyclophosphamide but with fewer adverse events. The EVER-ILD trial[17] demonstrated that combining MMF with rituximab improved FVC and progression-free survival compared with MMF alone in patients with an NSIP pattern of disease. In RA-ILD, initial therapeutic decisions are dictated based on whether active arthritis is present. When active arthritis exists, EULAR/ERS conditionally recommend abatacept, rituximab, or Janus kinase inhibitors.[2] Despite their underlying immunologic pathogenesis, identifying a PPF phenotype in CTD-ILD remains critically important because of its distinct prognostic significance and therapeutic implications. In a Canadian cohort study, 45% of patients with CTD-ILD developed evidence of PPF within 24 months of their diagnosis.[18]

Interstitial Lung Abnormalities

Interstitial lung abnormalities (ILAs) refer to incidental HRCT findings characterized by non-dependent ground-glass opacities, reticulation, traction bronchiectasis, or subpleural fibrotic changes involving at least 5% of a lung zone in individuals without a known diagnosis of ILD. The 2025 ATS/ERS Clinical Statement highlights that ILAs are increasingly detected in lung cancer screening cohorts and in relatives of patients with familial pulmonary fibrosis.[19]

Risk factors for progression include advanced age, prior smoking history, subpleural reticulation, and fibrotic features. However, major uncertainties remain: the natural history varies, surveillance intervals are not standardized, and therapeutic implications remain unclear. Whether early antifibrotic therapy benefits high-risk ILAs remains unknown. For the practising respirologist, ILAs should prompt a structured clinical evaluation, baseline PFTs, and risk-adapted follow-up, especially in individuals with CTD, relevant exposures, or a family history of pulmonary fibrosis.

Future Directions

The next phase of ILD management will likely integrate multi-omic risk profiling with clinical phenotyping to enable personalized therapy. Epigenetic clocks and circulating fibroblast activation markers may soon complement telomere length as indicators of disease behaviour. Novel agents targeting alternative fibrotic pathways are entering phase 2 trials, while inhaled delivery platforms promise improved safety and adherence. Expanding access to antifibrotics and biologics across Canada will determine whether these innovations translate into improved outcomes.

Conclusion

By 2025, ILD care has evolved from a single-disease paradigm to an integrated, phenotype-guided approach. Radiographic patterns, immune profiles, and cellular-senescence markers

collectively define prognosis and therapeutic responsiveness. Emerging evidence from the FIBRONEER trial establishes nerandomilast as a promising antifibrotic with a potential mortality benefit, while the RECITAL, EVER-ILD, and focuSSced trials consolidate the role of biologic immunomodulation in CTD-ILD. For Canadian clinicians, the challenge lies not in scientific uncertainty but in equitable implementation—ensuring that all patients with ILD gain timely access to recommended therapies. Through informed diagnostics, evidence-based treatment, and continued advocacy, our respiratory community remains central to improving outcomes in this complex and rapidly advancing field.

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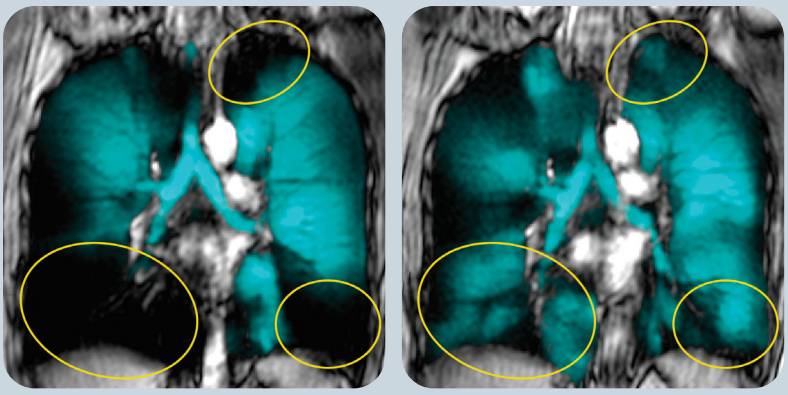

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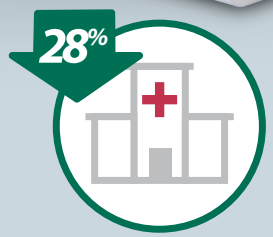

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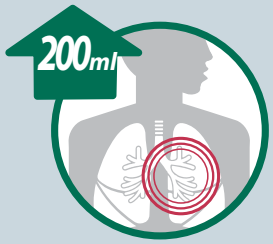

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Updates in Allergic Bronchopulmonary Aspergillosis

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Introduction

Allergic Bronchopulmonary Aspergillosis (ABPA) is a complex lung disorder that results from a hypersensitivity reaction to the fungus Aspergillus fumigatus following airway colonization in patients with chronic lung diseases. ABPA predominantly affects patients with asthma and cystic fibrosis, though it can occur in other bronchiectatic conditions. Worldwide, APBA is estimated to impact over four million people.[1,2]

The pathogenesis of APBA involves both type I and type III hypersensitivity reactions, creating a distinctive inflammatory cascade dominated by T-helper 2 (Th2) lymphocytes and eosinophils. This immune dysregulation leads to recurrent mucoid impaction, progressive bronchiectasis, and, if left untreated, irreversible lung damage.[2] As our understanding of ABPA pathophysiology has evolved, therapeutic approaches have advanced significantly, with biologic therapies offering promising steroid-sparing alternatives for refractory or steroid-dependent diseases.

The clinical presentation of ABPA often overlaps with poorly controlled asthma, making diagnosis challenging and frequently delayed. Patients typically present with worsening asthma symptoms, a productive cough containing brownish mucus plugs, and occasionally hemoptysis. Acute exacerbations may also be accompanied by constitutional symptoms, such as low-grade fever and malaise. The hallmark of ABPA is its tendency toward recurrent exacerbations interspersed with periods of relative stability.[3]

The 2024 guidelines from the International Society for Human and Animal Mycology (ISHAM) define distinct clinical states to guide management. Acute ABPA encompasses both newly diagnosed cases meeting diagnostic criteria and exacerbations in known patients, characterized by sustained clinical or radiological worsening with a 50% or more increase in serum total IgE from baseline stability values. Response to treatment is defined by at least 50% symptomatic improvement combined with either major radiological improvement or a 20% decline in IgE after 8 weeks. Remission requires sustained clinico-radiological improvement for at least 6 months without glucocorticoids and without a 50% rise or more in IgE levels; patients receiving biologics or long-term antifungal therapy may also achieve remission meeting these criteria. Treatment-dependent ABPA occurs when patients experience two or more consecutive exacerbations within 3 months of discontinuing glucocorticoids or develop worsening symptoms with imaging changes or IgE elevation within 4 weeks of steroid tapering on two separate occasions. Advanced ABPA is characterized by extensive bronchiectasis involving ten or more segments, accompanied by the development of cor pulmonale or chronic type 2 respiratory failure.[3] Recognizing these clinical states guides treatment intensity and monitoring frequency.

Diagnosis

The ISHAM working group published revised clinical practice guidelines in 2024, providing updated diagnostic criteria.[3]

Diagnostic Criteria

A diagnosis of ABPA requires three essential components:

1. A predisposing condition such as asthma, cystic fibrosis, chronic obstructive lung disease, or bronchiectasis, or compatible clinical features including expectoration of mucus plugs, fleeting pulmonary opacities, or finger-in-glove opacities on imaging.
2. Sensitization to *Aspergillus fumigatus* demonstrated by a positive skin test or elevated specific IgE.
3. Evidence of immunologic activity with elevated total serum IgE (typically ≥500 IU/mL in

asthmatic patients, though lower thresholds apply in cystic fibrosis).[3]

Additional supportive features that strengthen (but are not essential to) the diagnosis include: positive IgG against *Aspergillus fumigatus*, peripheral blood eosinophilia ≥500 cells/μL, and characteristic radiographic abnormalities.[3]

Radiological Features

Chest radiographs may demonstrate fleeting opacities or the pathognomonic finger-in-glove sign. High-resolution computed tomography (CT) offers greater sensitivity, typically revealing central bronchiectasis (affecting proximal airways), mucus plugging, and tree-in-bud opacities. The presence of high-attenuation mucus on CT is considered pathognomonic for ABPA and can independently confirm the diagnosis, even when other criteria are not fully met.[3,4]

Treatment

Overview and Goals

The therapeutic approach incorporates anti-inflammatory medications, such as corticosteroids or biologics targeting type 2 immune pathways, to modulate immune activity, and antifungal therapy to reduce the fungal burden in the respiratory tract. Treatment goals include relieving clinical symptoms, achieving optimal asthma control, preventing exacerbations, halting the progression of bronchiectasis, and minimizing treatment-related adverse effects.[3,5]

Corticosteroids

Systemic corticosteroids remain the cornerstone of ABPA treatment. Oral prednisolone effectively suppresses the inflammatory cascade, reduces serum IgE levels, resolves pulmonary infiltrates, and improves clinical symptoms. The standard regimen involves initiating treatment with oral prednisolone at 0.5–0.75 mg/kg/day for 2–6 weeks, followed by gradual tapering over 3–6 months while monitoring clinical response, pulmonary function, and IgE levels.[3,5] High-dose inhaled corticosteroids alone are insufficient for acute ABPA but play an important and necessary role in maintenance asthma management.

Despite its effectiveness, corticosteroid therapy has significant limitations. Many patients require prolonged or repeated courses, which can lead to complications including weight gain, hyperglycemia, osteoporosis, increased infection risk, and adrenal suppression. In some cases, patients become steroid-dependent or develop steroid-refractory disease, necessitating alternative therapies.[6] These concerns have driven the search for effective steroid-sparing agents.

Antifungal Agents

For patients who cannot tolerate corticosteroids or fail to taper oral prednisolone, oral antifungal azoles serve as important alternatives. Oral itraconazole, the most studied antifungal in ABPA, reduces fungal burden and antigen load. It is typically dosed at 200 mg twice daily for 16 weeks or longer. Studies demonstrate that itraconazole can reduce corticosteroid requirements, decrease exacerbation frequency, and improve pulmonary function and quality of life.[5,6]

Essential monitoring includes measuring serum itraconazole levels to ensure adequate absorption, performing hepatic function tests, and assessing for drug interactions. Voriconazole and posaconazole represent alternatives for patients intolerant to itraconazole, though supporting evidence is more limited. Routine first-line management of acute ABPA should not combine itraconazole with glucocorticoids; however, a brief glucocorticoid course of under 2 weeks may be administered alongside oral itraconazole at initiation.[3]

Biologic Therapies

Recognizing ABPA as a Th2-mediated eosinophilic disease has opened the door for targeted biologic therapies that offer disease control while minimizing corticosteroid exposure. Although these biologic agents are approved for severe asthma, their use in ABPA remains off-label, though growing evidence supports their efficacy and safety in this population.

Anti-IgE Therapy: Omalizumab

Omalizumab, an anti-IgE monoclonal antibody, was the first biologic evaluated for ABPA. Studies have demonstrated its effectiveness in reducing exacerbations and enabling corticosteroid reduction.[7,8] However, omalizumab shows limited impact on radiological abnormalities such as bronchial mucus plugs. Additionally, the characteristically elevated serum IgE levels of ABPA (often >1000 IU/mL) frequently result in suboptimal dosing, as the maximum approved dose may provide insufficient IgE neutralization.[7]

Anti-IL-5 Pathway Therapies: Mepolizumab and Benralizumab

Therapies targeting interleukin (IL)-5 or its receptor are unaffected by IgE levels. IL-5 is the key cytokine responsible for eosinophil maturation, activation, and survival. Two antibody classes target this pathway: anti-IL-5 monoclonal antibodies (mepolizumab) and anti-IL-5 receptor-alpha chain antibodies (benralizumab).

Mepolizumab, typically administered subcutaneously at 100–300 mg every 4 weeks, blocks IL-5, preventing eosinophil recruitment and activation. Benralizumab, administered as 30 mg subcutaneously every 4 weeks for the first three doses, and then every 8 weeks, binds the IL-5 receptor-alpha expressed on eosinophils and basophils, inducing antibody-dependent cell-mediated cytotoxicity and causing rapid, near-complete eosinophil depletion.[9]

Studies demonstrate that both agents significantly reduce exacerbation frequency, improve forced expiratory volume in one second (FEV1), resolve radiological abnormalities (particularly mucus plugs), and provide substantial corticosteroid-sparing effects.[9,10,13] Notably, benralizumab may offer superior efficacy in clearing mucus plugs, with studies showing resolution rates of 82–100%, likely due to its more potent eosinophil-depleting mechanism.[9] Some patients with inadequate response to mepolizumab have achieved mucus plug clearance after switching to benralizumab.[9]

The choice between mepolizumab and benralizumab may be guided by several factors including dosing frequency preferences (every 4 weeks versus every 8 weeks after loading), cost and insurance coverage considerations, previous treatment responses, and clinician experience. Although both agents target the IL-5 pathway, benralizumab's mechanism of direct eosinophil depletion may be preferable in patients with markedly elevated eosinophil counts or those who respond inadequately to mepolizumab.

Anti-IL-4 Receptor Alpha Therapy: Dupilumab

Dupilumab, which blocks both IL-4 and IL-13 signalling, has shown promise in ABPA case reports. Interestingly, some mepolizumab-refractory patients have improved with dupilumab, suggesting that targeting different Th2 pathways may benefit distinct patient subgroups.[11] However, given that ABPA typically involves pronounced eosinophilia, dupilumab's safety profile warrants careful evaluation, as post-treatment eosinophilia could lead to complications.[9,11] Further studies are needed to establish its role in ABPA management.

Indications for Biologic Therapy

Not all ABPA patients require biologics. Ideal candidates include those with frequent exacerbations despite optimized conventional therapy, patients requiring maintenance oral corticosteroids or frequent bursts, those experiencing significant corticosteroid-related adverse effects, and patients with persistently elevated eosinophil counts and deteriorating lung function.[3,13]

Before initiating biologic therapy, clinicians should confirm an accurate diagnosis, optimize conventional management, including inhaled corticosteroids and bronchodilators, address comorbidities, and consider antifungal therapy. Baseline assessments should include pulmonary function tests, total IgE levels, peripheral eosinophil counts, and high-resolution CT imaging.[3]

Monitoring Treatment Response

Regular monitoring is essential. Clinical parameters include symptom control, exacerbation frequency, and corticosteroid requirements. Laboratory monitoring involves serial IgE levels (typically every 2–3 months initially, then every 6–12 months), though IgE may not decline proportionally to clinical improvement, emphasizing the importance of patient-centred outcomes.[9,11,13] Pulmonary function testing every 3–6 months provides objective assessment, while follow-up CT imaging at 6–12 months helps assess radiological response, particularly mucus plug resolution and bronchiectasis stability.[3,9,11,13]

The therapeutic benefit of biologics appears more pronounced in ABPA associated with asthma versus cystic fibrosis, particularly in reducing exacerbations and enabling steroid-sparing.[11,12] Current evidence derives primarily from case series and retrospective studies; rigorous randomized controlled trials are essential to definitively establish safety and efficacy.[11,13] Since omalizumab, mepolizumab, benralizumab, and dupilumab are approved for severe asthma, and most ABPA studies involve asthma patients, additional studies are needed to demonstrate efficacy specifically in ABPA with underlying cystic fibrosis.[12]

Conclusion

ABPA is a challenging clinical entity requiring prompt recognition and timely treatment to prevent significant morbidity. While corticosteroids and antifungal agents remain the foundation of treatment for ABPA, biologic therapies, although currently off-label, have transformed management for refractory or steroid-dependent disease. These targeted therapies offer effective disease control with acceptable safety profiles and steroid-sparing benefits, underscoring the importance of obtaining more rigorous evidence to support their role in ABPA management.

As biologics become more integrated into ABPA management, thoughtful patient selection, systematic monitoring, and vigilance for long-term effects are essential. The 2024 ISHAM guidelines provide an updated framework for diagnosis and management, though continued research will further refine therapeutic approaches.[3]

Familiarity with these emerging therapies and their appropriate application is essential for optimizing outcomes in this complex patient population.

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A.E.: None declared.

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Antifibrotics in Non-Idiopathic Pulmonary Fibrosis Interstitial Lung Diseases

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Case 1

A 73-year-old male with a history of seronegative rheumatoid arthritis associated interstitial lung disease (RA-ILD), showing a probable usual interstitial pneumonia pattern of fibrosis, was seen for follow up. He had initially been started on mycophenolate for treatment of his ILD and remained stable on this treatment for a period; however, he later experienced slowly worsening dyspnea and cough over time. His pulmonary function tests (PFTs) demonstrated a 9.5% relative and 6% absolute decline in forced vital capacity (FVC) and a 12% relative and 10% absolute decline in diffusion capacity for carbon monoxide (DLCO) over the past 20 months. A computed tomography (CT) scan of the thorax showed some new changes of mild honeycombing in the right lower lobe **(Figure 1)**.

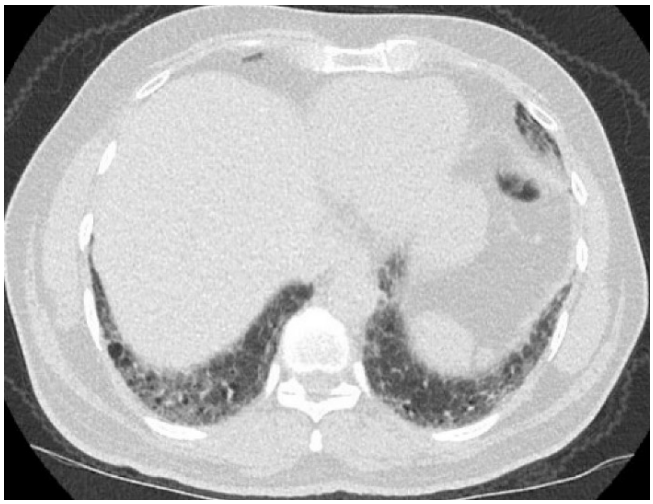

Figure 1. Axial view of recent CT thorax demonstrating new mild honeycombing in the right lower lobe; *courtesy of Yassmin Behzadian, MD, FRCPC, and Ambrose Lau, MD, MEd, FRCPC*

Case 2

A 50-year-old male developed dyspnea and cough after a COVID-19 infection. During the COVID-19 infection, his symptoms were mild and did not require treatment or hospitalization. A CT scan of the thorax demonstrated evidence of a fibrotic non-specific interstitial pneumonia pattern. Subsequent evaluation for new-onset ILD, included a surgical lung biopsy, which demonstrated organizing pneumonia with cicatricial changes.

The patient received a course of prednisone, which led to a significant improvement in his symptoms but no improvement in imaging or PFTs. After tapering off prednisone, he required another course due to re-emergence of symptoms. However, retreatment yielded no improvement in his symptoms, imaging, or PFTs. The patient's case, imaging, and pathology were reviewed in a multidisciplinary discussion, resulting in a diagnosis of organizing pneumonia evolving

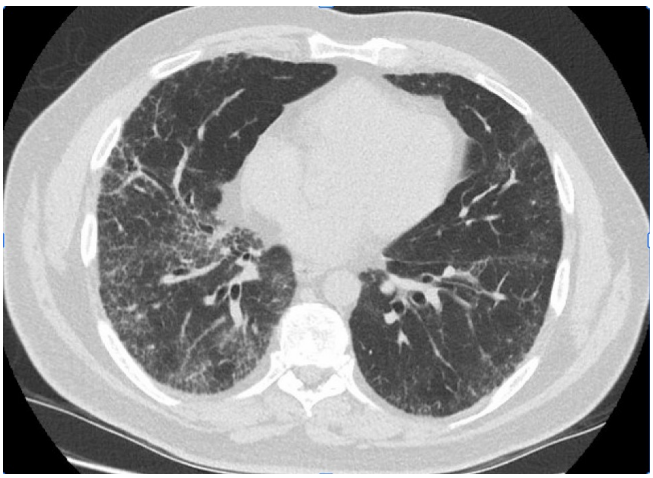

Figure 2. Axial view of recent CT thorax demonstrating increased reticulation; *courtesy of Yassmin Behzadian, MD, FRCPC, and Ambrose Lau, MD, MEd, FRCPC*

toward a more fibrotic phenotype. In addition to his worsening symptoms, imaging revealed increased reticulation, and assessments showed a significant decline in his FVC and DLCO over time.

Progressive Pulmonary Fibrosis

ILDs comprise a group of parenchymal pulmonary diseases with diverse causes and manifestations. In addition to Idiopathic Pulmonary Fibrosis (IPF), numerous other types of fibrotic ILDs exist. Progressive pulmonary fibrosis (PPF) is a possible disease course in these non-IPF fibrotic ILDs, characterized by progression over time.[1]

The 2022 American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), Asociación Latinoamericana de Tórax (ALAT) clinical practice guideline defines PPF as the presence of at least two out of three criteria occurring within the past year, with no other cause: 1) worsening respiratory symptoms, 2) physiological disease progression, and 3) radiological disease progression.[1] It is important to note that definitions of progression vary in the literature. For example, the INBUILD trial defined progression as any of the following occurring within the previous 24 months: a relative decline in FVC of ≥10% of the predicted value, a combination of a relative decline in the FVC of 5% to <10% of the predicted value combined with increased respiratory symptoms or fibrosis extent on high-resolution CT (HRCT), or increased respiratory symptoms and fibrosis extent on HRCT.[2] The 2022 ATS/ERS/JRS/ALAT clinical practice guideline defines physiological disease progression as either an absolute decline in FVC of ≥5% predicted or an absolute decline in DLCO (hemoglobin-corrected) of ≥10% predicted within 1 year.[1] A comparison of these and other criteria is outside the scope of this paper.

The reported prevalence of PPF varies across studies and is dependent on various factors, such as the definition of progression used and the type of ILD. A recent retrospective analysis noted a PPF prevalence of 40% when using the 2022 ATS/ERS/JRS/ALAT criteria.[3] Patients who experience progression have early mortality and an overall disease course that is similar to that of patients with IPF.[4]

The Use of Antifibrotics in Non-Idiopathic Pulmonary Fibrosis Interstitial Lung Diseases

The available antifibrotics currently approved for the treatment of IPF include nintedanib and pirfenidone, with the former also being approved by Health Canada for the treatment of PPF.

Nintedanib is an oral tyrosine kinase inhibitor that binds and blocks multiple receptors to ultimately suppress central processes involved in fibrosis.[5] The INPULSIS-1 and INPULSIS-2 trials assessed the role of nintedanib in the treatment of IPF, demonstrating that nintedanib reduced the annual rate of FVC decline compared to placebo.[6]

Subsequent studies have assessed the role of nintedanib in the treatment of patients with non-IPF ILDs. The SENSCIS trial was a randomized, double-blind, placebo-controlled, phase 3 study that evaluated the impact of nintedanib on the annual rate of FVC decline over 52 weeks in patients with systemic sclerosis associated ILD (SSc-ILD). Enrolled patients had at least 10% fibrotic lung involvement on high-resolution CT scans, among other inclusion criteria.[7] Patients treated with nintedanib experienced a significant reduction in the annual rate of FVC decline compared to placebo.[7] In the SENSCIS trial, 48.4% of patients were receiving background mycophenolate therapy at baseline.[7] A subsequent post hoc analysis found that nintedanib's effect on the attenuation of annual FVC decline was not significantly influenced by concomitant background mycophenolate therapy.[8]

The INBUILD trial, which was a randomized, double-blind, placebo-controlled phase 3 study, assessed the effect of nintedanib in patients with non-IPF fibrotic lung disease and evidence of progression. Patients who received nintedanib demonstrated a significant reduction in the annual rate of FVC decline compared to placebo.[2] A post hoc analysis of this trial suggested that nintedanib exerted a consistent effect on the annual rate of FVC decline across patients with the various ILD diagnoses included.[9] Diarrhea was the most frequently reported adverse event among patients receiving nintedanib in the INBUILD, INPULSIS, and SENSCIS trials.[2,6,7]

Pirfenidone is an oral antifibrotic currently used in the treatment of patients with IPF and has been shown to reduce disease progression in this patient population compared to placebo.10 The use of pirfenidone in patients with non-

IPF fibrotic ILDs has also been assessed. The RELIEF study suggested that pirfenidone may help reduce disease progression in patients with certain non-IPF fibrotic ILDs exhibiting evidence of progression.[11] In the TRAIL1 trial, the composite primary endpoint, defined as a decline in percent predicted FVC of at least 10% from baseline or death, was not significantly different between patients with RA-ILD receiving pirfenidone or placebo. However, patients with RA-ILD who received pirfenidone exhibited a lower annual rate of FVC decline.[12] Both these studies were terminated early due to various challenges, which limits the interpretation of results.[11,12]

Nerandomilast, an oral phosphodiesterase 4B inhibitor, has antifibrotic and immunomodulatory properties. Recent double-blind, randomized, placebo-controlled phase 3 trials demonstrated that nerandomilast attenuated FVC decline over 52 weeks compared to placebo in patients with IPF[13] as well as in patients with other fibrotic lung diseases showing evidence of progression.[14] In the latter population, 43.5% of patients were receiving background nintedanib.[14]

Review of Cases

In case 1, the patient demonstrated evidence of PPF based on worsening symptoms and radiological evidence of fibrotic progression. Additionally, there was a documented decline in both FVC and DLCO over time.

In patients with fibrotic ILD, nintedanib is often initiated in a stepwise approach. The 2022 ATS/ERS/JRS/ALAT clinical practice guideline suggests the use of nintedanib in patients with fibrotic lung disease with PPF who do not respond to standard management, which may include non-pharmacological and/or pharmacological strategies, and which will vary based on the underlying ILD and the specific context.[1]

In this case, initiation of antifibrotic therapy over increasing the patient's immunosuppressive therapy was recommended, as the patient exhibited evidence of a fibrotic ILD with fibrotic progression despite treatment, and no evidence of an alternative cause (e.g., poorly controlled inflammation) based on available investigations. For some patients with RA-ILD, who present with predominantly fibrotic disease at diagnosis, have already demonstrated progression, and who show minimal concern for an active inflammatory process, it may be reasonable to consider upfront initiation of nintedanib versus immunosuppressive therapy. However, the 2023 guideline from the American College of Rheumatology (ACR)/ American College of Chest Physicians (CHEST) on managing patients with systemic autoimmune rheumatic disease associated-ILD, a consensus was not reached regarding nintedanib as a first line treatment option in RA-ILD.[15]

In case 2, given the progression of the patient's symptoms, declining PFTs over time, and increased reticulation on imaging, antifibrotic treatment with nintedanib was recommended. Immunosuppressive therapy could also be reassessed in the future should the patient develop inflammatory changes or a connective tissue disease. Case 2 demonstrates the role of nintedanib in managing patients who have non-IPF fibrotic lung disease with PPF when no alternative cause is suspected. It also highlights the importance of multidisciplinary discussion in diagnosis and during management decisions, especially for patients with ILD.

Conclusion

For patients with non-IPF fibrotic lung disease, the current guideline recommends nintedanib for patients with evidence of PPF.[1] Pirfenidone has also been studied and shows supportive findings, though interpretation of the data is more limited. Nerandomilast, pending Health Canada approval, has shown a decrease in FVC decline compared to placebo in this patient population.[14]

The use of antifibrotics in patients with non-IPF fibrotic lung diseases should be individualized, taking into account the patient's clinical history, personal preferences, and, whenever possible, input from a multidisciplinary discussion.

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NOTE: Specific indications, contraindications, warnings, precautions and safety information exist for these products and therapies. Please consult a clinician and product instructions for use prior to application. Rx only.

As with any case study, the results should not be interpreted as a guarantee or warranty of comparable results. Individual results may vary depending on the patient's circumstances and condition.

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Management of Pulmonary Tuberculosis in 2025: An Update for the Respirologist

Natasha Sabur, MD, MPH, FRCPC

Background

Despite being a curable illness, tuberculosis (TB) remains the most common cause of death from an infectious agent, with a reported 10 million infections and 1.25 million TB-related deaths reported globally in 2023.[1] In Canada, the incidence of TB has remained at approximately 5.1 per 100,000 for many years.[2] However, foreign born and Indigenous populations are disproportionately affected by TB, with the Inuit population experiencing the highest TB incidence in Canada, at a reported rate of 70 per 100,000 in 2020.[3] Drug-resistant TB is reported in less than 10% of TB isolates in Canada, the majority being isoniazid mono-resistant. Multidrug-resistant TB (MDR-TB), defined as resistance to both isoniazid (INH) and rifampin (RIF), is detected in fewer than 4% of drug-resistant TB isolates in Canada.[3]

TB is caused by the *Mycobacterium tuberculosis* (MTB) bacillus, and is spread when people infected with TB aerosolize the bacteria through coughing, laughing, singing, or talking. Following initial infection, the risk of developing active TB disease is greatest in the first 2 years, then decreases significantly, with an estimated lifetime risk of approximately 10%.[4] In addition to several host factors, the risk of TB reactivation increases in the setting of immune suppression, including HIV infection, malignancy, organ or bone marrow transplant, and immunosuppressive treatments such as prednisone and tumour necrosis factor (TNF)-alpha therapy.[5] Prior to initiating treatments that may increase the risk of reactivation, latent TB infection should be considered and appropriate investigations performed.

Diagnosis

TB Infection

An estimated 2 billion people globally have latent tuberculosis infection (LTBI) and are at risk of reactivation of TB disease.[1] Screening is indicated for those who are deemed to have a higher risk of reactivation and in whom there is an intention to treat latent infection if positive. LTBI is diagnosed with either a tuberculin skin test (TST) or an interferon gamma release assay (IGRA). In most Canadian settings, the TST is favoured due to wider availability and lower cost. However, the TST can yield false positive results in individuals who have previously received the bacille Calmette-Guérin (BCG) vaccine,[6] making IGRA the preferred test in this population.[7] BCG vaccination is currently administered to children in over 100 countries and in some Indigenous communities, resulting in a high prevalence in the Canadian foreign-born population and many Indigenous Canadians.

TB Disease

Chest X-ray and other imaging modalities are used to screen for active TB disease. However, the diagnosis of TB disease relies on three technologies: microscopy (sputum smear), molecular testing including nucleic acid amplification testing (NAAT), and culture-based methods.

Sputum smear microscopy remains the standard first-line test for TB disease in Canada. Although its sensitivity is poor, yield improves when multiple samples are collected and sputum induction is used.[8,9] The Canadian TB guidelines recommend that at least three sputum samples be collected, ideally 5–10 mL each, as this increases the yield for both smear and culture.[10] In most Canadian laboratories, a positive sputum smear

TPT Regimen	Dose	Duration of Therapy	Adverse Events
Rifampin monotherapy (4R)	10 mg/kg daily (maximum dose 600 mg/day)	4 months	Bone marrow suppression, rash, drug-drug interactions
Isoniazid monotherapy (9H)	5 mg/kg daily (maximum dose 300 mg/day)	9 months	Peripheral neuropathy, hepatotoxicity
Rifapentine and isoniazid (3HP)	Rifapentine: 10–14 kg – 300 mg weekly 14.1–25 kg – 450 mg weekly 25.1–32 kg – 600 mg weekly 32.1–49.9 kg - 750 mg weekly >= 50 kg - 900 mg weekly (maximum dose 900 mg/week) Isoniazid 15 mg/kg weekly (maximum dose 900 mg/week)	3 months (12 doses)	Hypersensitivity reaction, bone marrow suppression, drug-drug interaction
Isoniazid monotherapy (6H)	5 mg/kg daily (maximum dose 300 mg/day)	6 months	Peripheral neuropathy, hepatotoxicity
Isoniazid and rifampin (3HR)	Isoniazid: 5 mg/kg daily (maximum dose 300 mg/day) Rifampin: 10 mg/kg daily (maximum dose 600 mg/day)	3 months	Peripheral neuropathy, hepatotoxicity, rash, drug-drug interactions

Table 1. TB Preventive Therapy (TPT) regimens and side effects; *courtesy of Natasha Sabur, MD, MPH, FRCPC*

triggers NAAT testing to confirm the presence of MTB DNA. In many Canadian settings, the high prevalence of nontuberculous mycobacteria may further reduce the specificity of sputum smear sampling for pulmonary TB,[11] making NAAT testing critical for rapidly identifying those who may require respiratory isolation. Globally, the Xpert MTB/RIF technology (Cepheid Inc, Sunnyvale, California, USA), an automated NAAT that has demonstrated superior accuracy compared to smear microscopy and additionally provides rapid genotypic drug resistance information, is recommended by the World Health Organization (WHO) as the first-line test for patients with suspected TB.[12] Although not widely available across Canada, Xpert MTB/RIF technology is used in many Northern communities, and other forms of NAAT technology are used in many Canadian mycobacterial laboratories.

Automated liquid culture is generally regarded as the gold-standard confirmatory test for diagnosing active TB disease. Once a TB isolate has been cultured, phenotypic drug susceptibility to all first-line TB medications can be performed. However, many laboratories employ other methods to detect mutations known to confer drug resistance (genotypic drug susceptibility testing), as these methods provide detection of drug resistance more quickly than phenotypic methods. The Canadian TB guidelines recommend rapid molecular testing to predict drug-resistant TB for all samples with a new positive NAAT or culture for TB.[10]

TB Preventive Therapy (TPT)

TPT, or treatment for latent TB infection, reduces the risk of progression from infection to active disease and is recommended for individuals at high risk for reactivation. A landmark randomized controlled trial in the 1960's established the efficacy of isoniazid (INH) monotherapy for TPT,[13] and for decades, 9 months of INH monotherapy was considered the gold standard for TPT. However, INH monotherapy has notable limitations, including poor treatment completion rates and a significant adverse event profile. **Table 1** provides information on TPT regimens and side effects.

Subsequent studies have successfully evaluated other LTBI regimens— including 4 months of daily rifampin (RIF)[14] and 3 months of weekly high-dose INH and rifapentine[15] — for non-inferiority against 9 months of INH, and these are now recommended for TPT. Although the Canadian TB guidelines recommend 3HP (INH

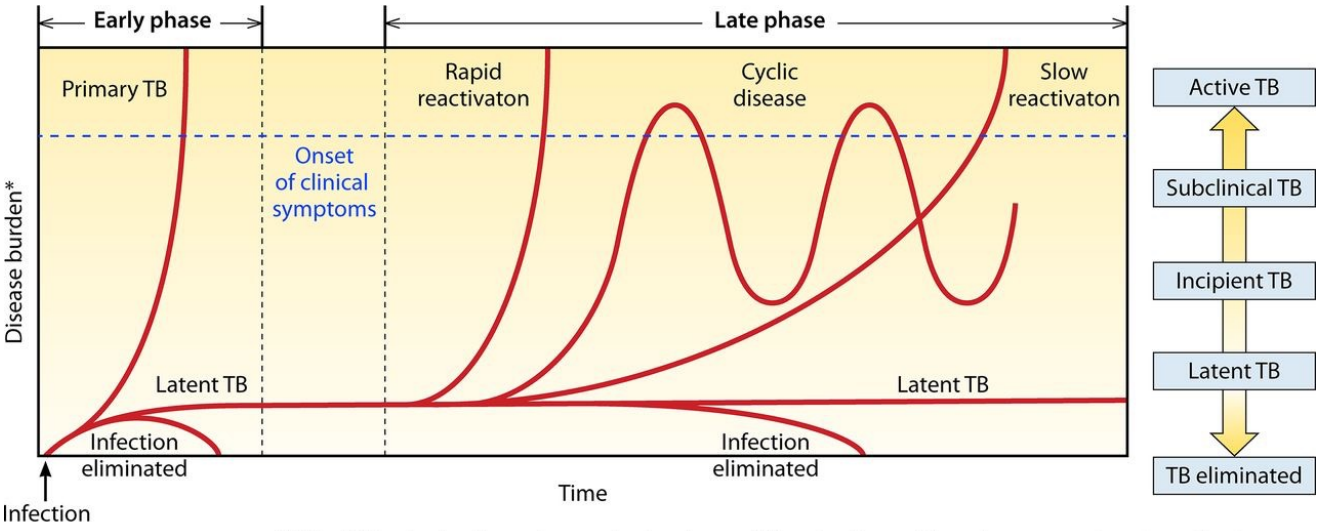

Figure 1. Pathways of tuberculosis disease progression. After initial exposure, *M. tuberculosis* may be eliminated by the host immune response, persist as a latent infection, or progress to primary active disease. Following the establishment of latent infection, disease may persist in a latent form, naturally progress in a slow or rapid fashion to active tuberculosis, or cycle through incipient and subclinical states before developing into symptomatic disease or eventual disease resolution. Although not all possibilities for regression of disease burden are depicted, spontaneous recovery may occur in any of these clinical trajectories; *used with permission from Drain, P. et al., 2018*

+ rifapentine) as the first-line TPT regimen,[16] rifapentine has not been approved by Health Canada, and significant drug access issues persist in many parts of Canada. An alternative regimen of 4 months of RIF is more widely used, with other treatment regimens considered when necessary.

Subclinical TB

Disease progression after infection has historically been divided into two forms: latent TB infection (asymptomatic, non-replicating bacteria, culture negative, non-infectious) and active TB disease (symptomatic, replicating bacteria, culture positive, infectious). We now have a better understanding of a more nuanced spectrum of TB infection, including a subclinical form of disease where patients are asymptomatic but harbour actively replicating TB bacilli with positive sputum cultures **(Figure 1)**. Radiographic findings in subclinical TB tend to be more subtle due to its paucibacillary nature, and since patients are asymptomatic, they may have more difficulty producing sputum for diagnosis. Furthermore, sputum smear and NAAT testing may have reduced sensitivity in subclinical TB resulting in delayed diagnosis.[17,18] TB prevalence data suggest that subclinical TB accounts for up to 50% of cases in endemic areas,[19] though its incidence in low burden settings such as Canada remains unknown. Emerging evidence suggests that subclinical TB may be intermittently infectious,[20] therefore contributing to community transmission and hampering global TB elimination efforts.

Treatment of TB disease

Drug-sensitive TB (DS-TB)

The recommended treatment regimen for drug-sensitive TB, developed more than four decades ago, consists of 6 months of rifampin (R) and isoniazid (H) with pyrazinamide (Z) added for the first 2 months and ethambutol (E) included until the isolate is known to be fully susceptible to first-line medications (commonly referred to as the HZRE regimen).

Although the standard 6 month regimen is safe and effective, its length is associated with nonadherence and loss to follow up, prompting efforts to shorten the duration of treatment for DS-TB. Several trials have attempted to reduce treatment duration with the addition of fluoroquinolones or with higher doses of RIF, however, none have shown non-inferiority to the HZRE regimen.[21-24] Rifapentine, a cyclopentyl derivative of rifampin with a longer half-life, has been evaluated in the context of treatment shortening. The TBTC Study 31/A5349, a randomized, open-label, phase 3 non-inferiority trial, demonstrated that a 4-month regimen consisting of isoniazid, rifapentine (P), moxifloxacin (M), and pyrazinamide (HPMZ) was non-inferior to the standard 6-month HZRE regimen in patients with DS-TB.[25] This regimen has been endorsed in international clinical practice guidelines as the first-line treatment for patients with drug-sensitive pulmonary TB in 2024.[26] In the Canadian setting, limited access to rifapentine has hindered broad uptake of this shorter-course treatment regimen. Additionally, there have been concerns regarding the high pill burden and poor tolerability of this regimen in clinical practice.[27] While research in this area continues, the standard 6-month HRZE regimen remains the gold-standard treatment for DS-TB.

Multidrug-resistant TB (MDR-TB)

Significant gains have been made in the treatment of MDR-TB. Previously, the standard treatment for MDR-TB consisted of up to 18 months of therapy, with significant toxicity and high rates of adverse events. Today, most cases of pulmonary MDR-TB can be treated with a 6-month, all-oral regimen known as the BPAL-M regimen, comprised of bedaquiline, pretomanid, linezolid, and moxifloxacin. This regimen is now endorsed by the WHO as the first-line treatment for MDR-TB.[28] Pulmonary MDR-TB is a rare disease in Canada, and treatment should be undertaken in consultation with a TB program experienced in managing drug-resistant TB.

Conclusions

TB continues to have a major impact on global health, and in Canada, continues to disproportionally affect the foreign born, Indigenous communities, and other vulnerable populations. Accumulating evidence suggests that subclinical TB may be an important contributor to TB transmission, though more research in this area is needed. Recent advances in the treatment of both drug-sensitive and drug-resistant TB may offer a more nuanced approach to treatment of pulmonary TB in years to come.

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