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Immune-Mediated Inflammatory Diseases and Their Clinical Management

A guide to immune-driven inflammatory diseases, their prevalence, manifestation, and interrelationships

Immune-mediated inflammatory diseases (IMIDs) constitute a heterogeneous group of seemingly unrelated disorders that share common inflammatory pathways and pathogenic mechanisms[1]

In IMIDs, the immune system is dysregulated, chronically active, and damaging to multiple organs and tissues[1]

Examples of IMIDs based on affected body regions[2]

Skin
Psoriasis, atopic dermatitis (AD), vitiligo, and alopecia areata (AA)

Intestines
Inflammatory bowel disease (IBD) that includes Crohn's disease (CD) and ulcerative colitis (UC)

Musculoskeletal system
Psoriatic arthritis (PsA), rheumatoid arthritis (RA), and spondyloarthritis (SpA)

Respiratory system
Asthma

Endocrine system
Type 1 diabetes mellitus and autoimmune thyroid diseases

Nervous system
Multiple sclerosis (MS)

Imbalance in inflammatory cytokines is the primary cause of pathogenesis[1]

Prevalence of IMIDs

Prevalence of IMIDs in Western society is 5–7%[1]

The Global Burden of Diseases, Injuries, and Risk Factors Study reported a global increase in the number of incident cases of IMIDs from 1990 to 2019[3]

Increased IMID incidence is attributed to:

Ageing

Environmental factors

Genetic risk factors

Obesity

Population growth

Societal development

The hygiene hypothesis postulates that reduced exposure to infectious agents increases the incidence of IMIDs[4]

Exposure to environmental air pollution is associated with a 10% higher risk of developing IMIDs[5]

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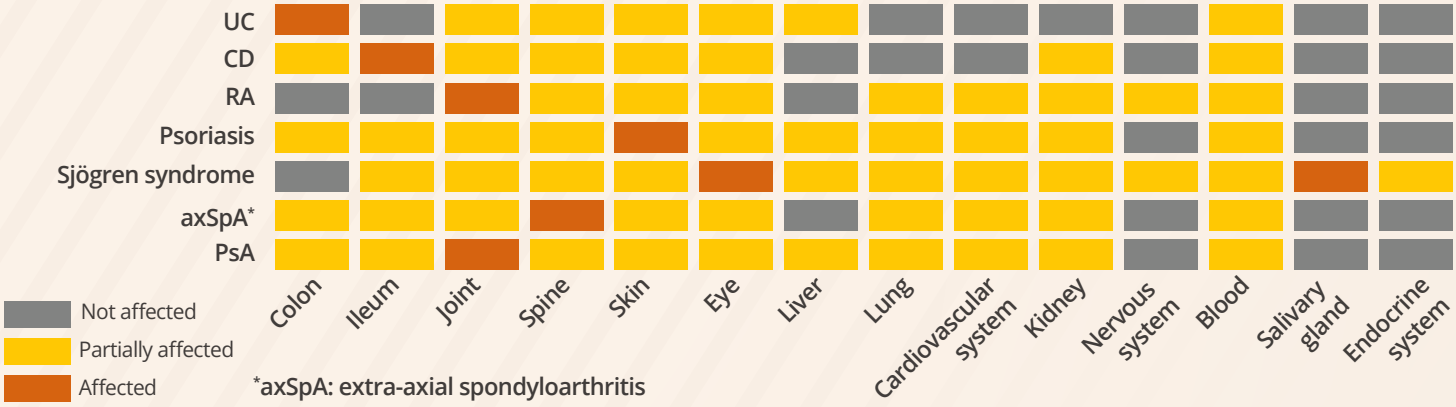
Inter-relationship between IMIDs

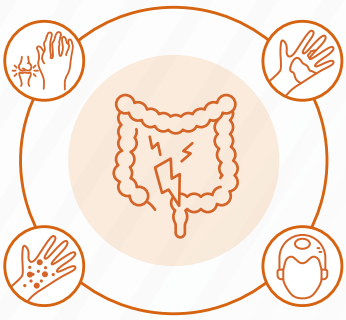
Patients with certain IMIDs, e.g., IBD and SpA, are more likely to develop another IMID[1,6]



Patients with concurrent IMIDs exhibit high disease severity[7]

For example, clinical progression is worse when the diagnosis of another IMID precedes that of IBD, as in 80% of cases in a Danish cohort[8]

MS, vitiligo, psoriasis, hypothyroidism, and RA were associated with increased AA risk[10]



IBD patients have an increased risk of developing skin disorders, e.g., hidradenitis suppurativa, psoriasis, AD, and neurological disorders, including MS[7,9]

Skin depigmentation disorder (vitiligo) is associated with a high risk of AD [odds ratio 7.8] and AA is associated with AD [odds ratio 2.57][11]

Extra-axial and extraintestinal manifestations

Extraintestinal manifestations (EIMs) in patients with IBD are inflammatory events located outside the gut, for which the pathogenesis is an inflammatory, environmental, or genetic predisposition common with IBD[12,13]

Most patients with SpA and PsA have a history or increased risk of developing inflammation in regions other than the spine and hips, referred to as extra-articular manifestations[14]

EIMs are IMIDs that commonly involve different types of tissues[13]

Prevalence in patients with IBD

Joints: 6–46%
(peripheral and axial spondyloarthropathies)

Skin: 5–15%
(erythema nodosum and pyoderma gangrenosum)

Eyes: 2–7%
(uveitis, episcleritis, and iridocyclitis)

Hepatobiliary tract: 5%
(primary sclerosing cholangitis)

Fatigue and pain: 50–70%

- EIMs can occur before (24%) or after the diagnosis of IBD[13]
- >10% of patients with IBD report three or more different EIMs[13]

Prevalence in patients with axial SpA[14]

Enthesitis: 35–60%

Psoriasis: 10%

IBD: 4–6%

Uveitis 6–30%

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Comorbidities contribute to the disease burden, put demands on the healthcare system, and impair patient's quality of life (QoL)[15–17]

AD is linked to lower overall health rating, life satisfaction, and impaired QoL related to mental health and skin concerns, especially in moderate to severe cases involving itching, since it adversely affects sleep, participation in activities, clothing choices, and social interactions in children and young adults[18,19]

Around 50% of patients with IBD in Europe exhibit some form of EIMs, which in turn adversely impacts patients' QoL and can be potentially life-threatening, besides adding to the healthcare burden[20]

Patients with RA experiencing an increase in disease activity exhibited decreased health-related QoL and increased disease burden in everyday life[21]

How are IMIDs inter-related?

IBD Psoriasis[9]

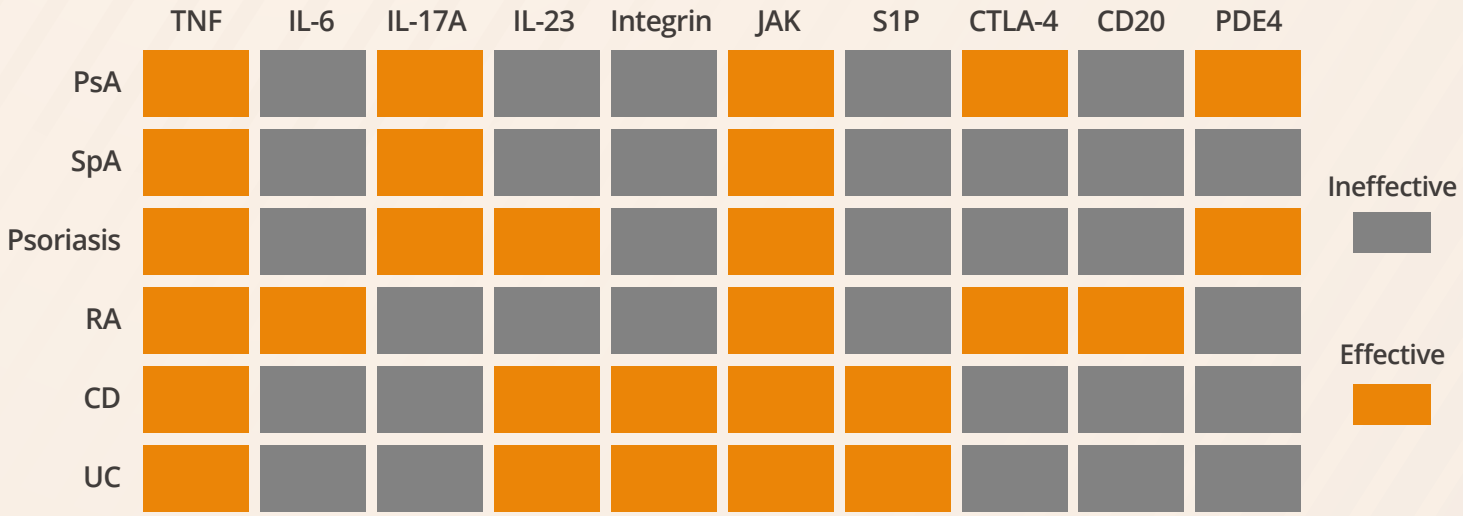
A Danish nationwide study shows an increased risk of IBD development in patients with psoriasis (higher in females than males and in the younger age group <30 years of age)

IBD and psoriasis share the IL-23, IL-17, JAK-STAT, and TNF proinflammatory signalling pathways

AD Asthma

AD and asthma share an active underlying type 2 inflammatory cytokine (IL-4/IL-13/IL-25) signalling[22]

Effectiveness of targeting signature molecules of IMIDs[6]



CD20: cluster of differentiation 20; CTLA: cytotoxic T-lymphocyte associated protein; IL: interleukin; JAK: Janus kinase; PDE: phosphodiesterase; S1P: sphingosine-1-phosphate; TNF: tumor necrosis factor

- Anti-TNF therapy is effective for patients with concurrent IMIDs, such as RA, axSpA, IBD, and PsA[6]
- Anti-IL-17A therapy is efficacious for patients with psoriasis, AS, or PsA[23]
- Anti-IL17A therapies indicated for treating MS and IBD often cause opportunistic infections[26]; currently, only a class of sphingosine-1 receptor modulators have a known role in MS and IBD[9]

A multidisciplinary approach can identify correct therapies, prevent complications, and improve both clinical outcomes and QoL[24]

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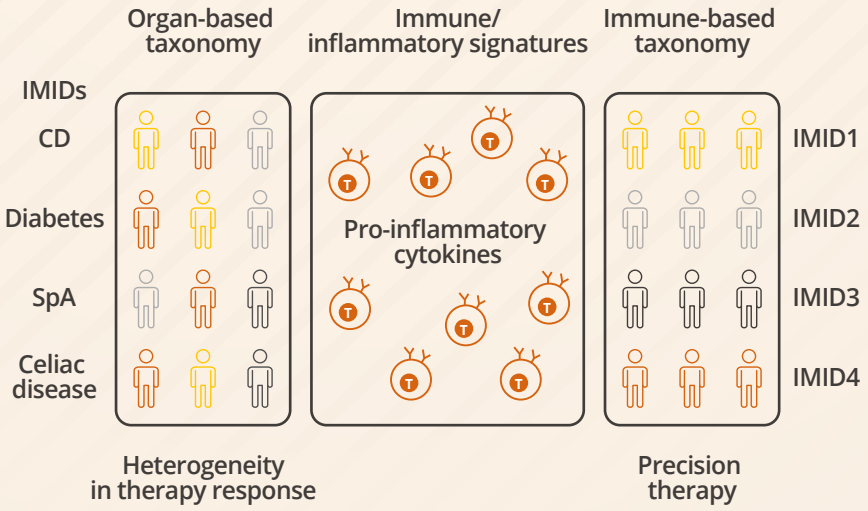
Recommendations for the appropriate clinical management of IMIDs[24]

- Active screening for IMIDs at first contact
- Be watchful for signs and symptoms of concomitant IMIDs
- Clinical awareness regarding the inter-relationship between IMIDs can avoid diagnostic delays

Molecular taxonomy or clustering of IMIDs based on common immunological pathways[2,25]



- Classifying IMIDs based on molecular features or biomarkers is a novel approach unlike conventional approaches, which evaluates affected organs
- Advanced molecular approaches involving single-cell RNA-sequencing and multi-omics data can yield detailed immunological information and aid in more accurate classification
- Molecular profiling across IMIDs can match the right drug to the right tissue in the right patient

Key message

Clinical awareness of IMIDs, their symptoms, and common immunopathogenic pathways, along with a multidisciplinary approach to clinical care can improve the diagnosis, management, comorbidities, and QoL associated with IMIDs

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