MEDICATION MANAGEMENT IN AGED CARE WHILE MITIGATING COVID-19

IMMUNODEFICIENCY

The Australian Government Department of Health has stated that the following groups of people are at high risk of severe illness with COVID-19 (coronavirus):

- those who are 70 years of age or over
- those who have had an organ transplant and are on immune suppressive therapy
- those who have had a bone marrow transplant in the last 24 months
- those who are on immune suppressive therapy for graft versus host disease
- those who have blood cancer e.g. leukaemia, lymphoma, or myelodysplastic syndrome (diagnosed within the last five years)
- those who are having chemotherapy or radiotherapy.[1]

Other than age, all of these factors are associated with acquired or existing immunodeficiency. Information for patients, consumers and carers regarding COVID-19 and immunodeficiency is available from the Australasian Society of Clinical Immunology and Allergy.[2]

KEY POINTS

While immunosuppression may increase risk of infection with COVID-19, immunosuppression during the acute hyperinflammatory state may be beneficial.

Doses of prednisolone below 10mg daily (without concurrent other immunosuppressives) do not seem to pose an additional risk in COVID-19.

As a general principle for the management of autoimmune conditions, maintaining immunosuppressive therapy at the minimum effective dose remains an appropriate strategy.

In aged care facilities, the number of patients with bone marrow transplants and/or having active chemotherapy or radiotherapy is very low. There are a significant number, however, who have had organ transplants (usually renal transplants) or who have a haematological malignancy.

In addition to factors associated with a high risk of severe illness with COVID-19, the Australian Government Department of Health includes some chronic inflammatory conditions and treatments and other primary or acquired immunodeficiency as having a moderate risk of severe illness with COVID-19.[1] Although primary immunodeficiency disorders (primary antibody deficiencies such as hypogammaglobulinaemia) are rare in aged care settings, many patients have inflammatory conditions such as rheumatoid arthritis or inflammatory bowel disease, and patients are often receiving systemic corticosteroids for these and other conditions.

Two phases of COVID-19 are generally recognised: an initial viral infection and replication phase, and a subsequent immune response phase characterised by often severe hyperinflammation and possible acute respiratory distress (see **Figure 1**). Thus, while immunosuppression may increase risk of infection with the virus (and co-infection with other microbes), immunosuppression during the acute hyperinflammatory state is often beneficial.

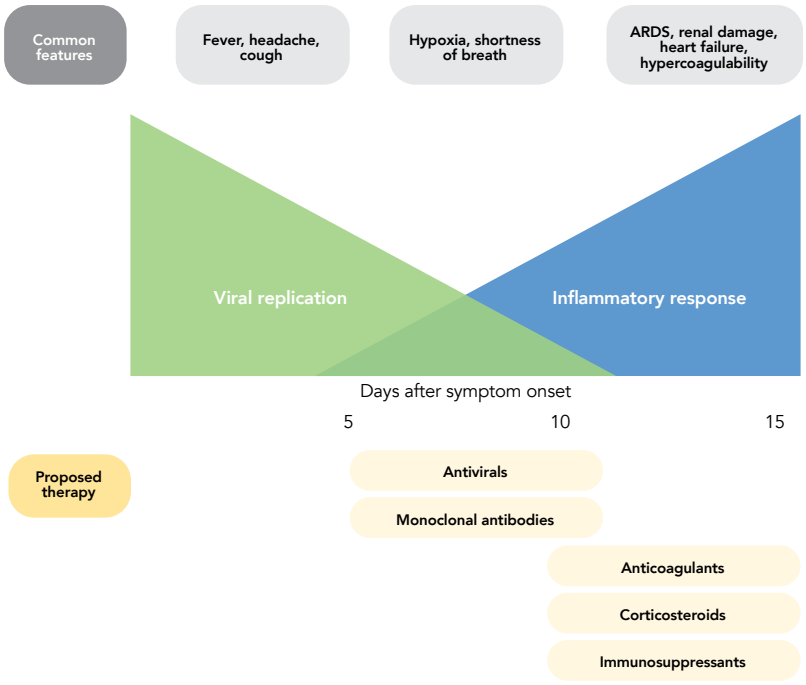

Figure 1: Two phases of COVID-19, typical symptoms and potential therapies (adapted from Reference 8)

RHEUMATOID CONDITIONS

The National Institute for Health and Care Excellence (NICE) has released a COVID-19 rapid guideline for rheumatological autoimmune and inflammatory disorders.[3] The guideline provides an evaluation of a range of conditions and their potential risk above that of the general population during COVID-19 (see **Table 1**). As can be seen, the more common conditions of rheumatoid or psoriatic arthritis and polymyalgia are less of a risk than temporal arteritis, systemic lupus erythematosus or scleroderma.

Many patients in aged care have multiple co-morbidities in addition to their autoimmune disease and may be taking immunosuppressive medications. While the underlying autoimmune disease may increase risk of contracting COVID-19, additional co-morbidities and immunosuppressive treatments are likely to contribute to poor outcomes in the event of COVID-19.[4,5,6]

Condition	Risk level		
	Intermediate	High	Very high
Polymyalgia rheumatic (PMR)			
Primary Sjogren's syndrome			
Ankylosing spondylitis or axial spondylarthritis			
Juvenile idiopathic arthritis (JIA)			
Overlap consecutive tissue disease (CTD)			
Psoriatic arthritis			
Rheumatoid arthritis			
Systemic lupus erythematosus			
Adult-onset Still's disease			
Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyangiitis			
Aortitis			
Autoinflammatory syndromes			
Behcet's disease			
Giant cell arthritis (GCA) or temporal arteritis			
Immunoglobulin G4-related disease (IgG4-RD)			
Myositis, polymyositis, dermatomyositis, antisynthetase syndrome			
Polyarteritis nodosa			
Relapsing polychondritis			
Systemic sclerosis scleroderma			
Takayasu arteritis			
Vasculitis (other)			
CTD-related interstitial lung disease, RA-related interstitial lung disease			
CTD-related pulmonary hypertension, RA-related pulmonary hypertension			
Fibrodysplasia ossificans progressive			
Severe kyphosis or scoliosis from rare bone diseases, for example, hypophosphatasia, type 1 osteogenesis imperfecta, Hajdu Cheney			
Severe osteogenesis (previously types 3 and 4) imperfecta (if mobility is restricted or chest wall shape or lung capacity are affected)			

Table 1: Risk for COVID-19 for various rheumatological conditions (adapted from Reference 3)

IMMUNOSUPPRESSIVE MEDICATIONS

While immunosuppressive medications may place people taking them at increased risk of viral and other infections, corticosteroids and several disease-modifying antirheumatic drugs (DMARDs) are now becoming a part of COVID-19 therapy.[7,8]

The risk level associated with different medications for rheumatological conditions has been assessed in the NHS England's clinical guide on the management of rheumatology patients and published in the NICE rapid guideline (see **Table 2**).[3]

Of the more commonly used agents in aged care, high-dose corticosteroids (20mg or more of prednisolone per day), methotrexate and leflunomide pose a higher risk than sulphasalazine or hydroxychloroquine.

Based on these guidelines, prednisolone doses below 10mg daily do not pose an additional risk with COVID-19. Maintenance prednisolone doses for many of the conditions in **Table 1** are often below 10mg daily, so continuation of therapy seems reasonable. For patients who are asymptomatic and have underlying relapsing/remitting conditions (such as polymyalgia), it may be possible to slowly reduce maintenance doses of steroids. An important issue is to ensure that sudden cessation of corticosteroids does not occur as, in addition to acute adrenal insufficiency issues, this often results in the need for additional corticosteroids at a later date.

As a general principle for the management of autoimmune conditions, maintaining immunosuppressive therapy at the minimum effective dose remains an appropriate strategy.

Condition	Risk level			
	Low	Intermediate	High	Very high
Apremilast				
Hydroxychloroquine				
Sulfasalazine				
Anakinra				
Baricitinib				
Tofacitinib				
Upadicitinib				
Adalimumab				
Azathioprine				
Certolizumab pegol				
Ciclosporin				
Etanercept				
Golimumab				
Infliximab				
Ixekizumab				
Leflunomide				
Methotrexate				
Mycophenolate mofetil				
Sarilumab				
Secukinumab				
Sirolimus				
Tacrolimus				
Tocilizumab				
Ustekinumab				
Abatacept				
Belimumab				
Prednisolone 10 mg to 19 mg per day (or equivalent) per day for more than 4 weeks monotherapy				
Rituximab				
Prednisolone 10 mg per day (or equivalent) or more for more than 4 weeks **with 1 other immunosuppressant**				
Cyclophosphamide				
Prednisolone 20 mg or more per day (or equivalent) for more than 4 weeks				

Table 2: Risk for COVID-19 with various medications used in inflammatory conditions (adapted from Reference 3)

RENAL TRANSPLANT RECIPIENTS

As the survival of renal transplant patients increases, more patients are eventually presenting to aged care. A key issue in this setting is modification of immune-modulating therapy either pre-emptively or in the event of a COVID-19 infection. An overview of recommendations for different immune-modulating therapies is provided in a state-of-the-art review by Daoud et al.[9]

Therapy	Summary points
Corticosteroids	• Do not stop suddenly • Benefits depend on timing in regard to viral replication and hyperinflammatory response - high doses early in infection may predispose to co-infection - use during active inflammatory response may be beneficial
Calcineurin inhibitors (e.g. Cyclosporin, Tacrolimus)	• May have a role in ameliorating cytokine storm • Continue at low dose if possible
Mycophenylate	• Reduce dose or discontinue only in severe COVID-19 infection

Table 3: Recommendations for common immunomodulatory therapy for kidney transplant recipients (adapted from Reference 9)

MANAGING IMMUNODEFICIENCY WHILE MITIGATING COVID-19 IN RENAL TRANSPLANT RECIPIENTS

Avoid high-dose corticosteroid maintenance doses

Long-term high-dose corticosteroids (10mg or greater prednisolone equivalent) may predispose to infection with COVID-19 and subsequent co-infection. Slow reduction of the dose to the minimum required to manage the underlying condition is an appropriate strategy.

Continue anti-rejection therapies

Maintenance anti-rejection immune-modulating therapies should be continued in the absence of a COVID-19 infection. If an infection occurs, modification of the dose and medication may be required.

DMARDs

Maintain therapy with methotrexate, sulphasalazine or hydroxychloroquine at minimum effective doses. Consider changing any intravenous biological DMARDs to subcutaneous formulations.

[1] *https://www.health.gov.au/health-alerts/covid-19/advice-for-groups-at-risk*

[2] Australasian Society of Clinical Immunology and Allergy. COVID-19 and Immunodeficiency (Updated 15th May 2020). Available *https://www.allergy.org.au/images/pcc/ASCIA_PCC_COVID-19_Immunodeficiency_2020.pdf* accessed 3/6/2021

[3] COVID-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders (NG167) – update 31st March 2021 available at *https://www.nice.org.uk/guidance/ng167* accessed 3/6/21

[4] D'Silva KM, Wallace ZS. COVID-19 and rheumatoid arthritis. Curr Opin Rheumatol. 2021 May 1;33(3):255-261. doi: 10.1097/BOR.0000000000000786. PMID: 33625043.

[5] Ladani AP, Loganathan M, Danve A. Managing rheumatic diseases during COVID-19. Clin Rheumatol. 2020 Nov;39(11):3245-3254. doi: 10.1007/s10067-020-05387-8. Epub 2020 Sep 8. PMID: 32895747; PMCID: PMC7476772.

[6] Roongta R, Ghosh A. Managing rheumatoid arthritis during COVID-19. Clin Rheumatol. 2020 Nov;39(11):3237-3244. doi: 10.1007/s10067-020-05358-z. Epub 2020 Sep 6. PMID: 32892311; PMCID: PMC7474575.

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[8] D'Silva KM, Wallace ZS. COVID-19 and Disease-Modifying Anti-rheumatic Drugs. Curr Rheumatol Rep. 2021 Apr 24;23(5):28. doi: 10.1007/s11926-021-00998-9. PMID: 33893890; PMCID: PMC8065312.

[9] Daoud A, Alqassieh A, Alkhader D, Posadas Salas MA, Rao V, Fülöp T, Soliman KM. Immunosuppression in kidney transplant recipients with COVID-19 infection - where do we stand and where are we heading? Ren Fail. 2021 Dec;43(1):273-280. doi: 10.1080/0886022X.2021.1876730. PMID: 33491531; PMCID: PMC7850379.

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