

Sarcoidosis key points

Kevin F. Gibson MD

Professor of Medicine

Medical Director

Dorothy P. and Richard P. Simmons Center for Interstitial Lung Disease

Natural History of Sarcoidosis

-Spontaneous remission, clinically inactive

Usually requires no treatment

-Transiently or Chronic active disease

**Treatment to prevent granulomas
formation and organ damage**

-Relapsing and Remitting-(often we fail to recognize)

Treatment to prevent disease relapses

***It is the Relapsing-Remitting disease that often
insidiously progresses and leads to end organ
destruction or transplantation.***

Corticosteroids

PRO

- Rapid improvement in symptoms
- Short-term improvement in Xray findings
- Acutely effective in most organ systems involved

CON

- Toxicity limits the long term dosing
- Not effective in controlling chronic active disease (can't keep on high enough dose)
- Not useful in preventing relapsing-remitting disease for same reason
- No proven long term benefits

Methotrexate

the upside

- Many small and large clinical trials over the past 30 years at multiple centers in multiple countries have shown it as an effective steroid-sparing agent and treatment for chronic inflammatory disease (psoriasis, rheumatoid arthritis, and sarcoidosis).
- Can be taken in effective doses that control inflammation and prevent relapses.
- Generally well-tolerated and can be taken for extended periods of time.
- Effective in most organ system disease (?central nervous system, ?liver disease)

Methotrexate

the downside

- Slow onset of action: can take from 2-6 months for it full anti-inflammatory effects to occur.
- Highly variable oral bioavailability. Sometimes not enough of an oral dose gets into the bloodstream. May need to switch to subcutaneous route.
- Extremely rare: Within 6 weeks of therapy, hypersensitivity pneumonitis can develop-
- Liver toxicity extremely rarely occurs beyond cumulative dose of 3 grams (takes 3 years or longer to get to this dose)

Antimetabolite therapy for sarcoidosis

	Level of evidence in sarcoidosis	Most common toxic effects (>1%)	Rare but important toxic effects
Methotrexate	Double-blind placebo-controlled trials, prospective case series, case reports	Nausea, mouth ulcers, leucopenia, hepatotoxicity, infections	Pneumonitis, teratogenic
Azathioprine	Prospective case series, case reports	Leucopenia, nausea, infections	Severe leucopenia, hepatotoxic effects, pancreatitis, skin cancer
Leflunomide	Double-blind placebo-controlled trials, prospective case series, case reports	Leucopenia, hepatotoxic effects, infections, alopecia	Pneumonitis, teratogenic, peripheral neuropathy, hypertension
Mycophenolate mofetil	Case series	Nausea, diarrhoea, infections	Skin cancer

- Baughman RP. Lancet Respir Med 2015

A Delphi Consensus Study

Sarcoid experts don't always agree!

Question #1: You determine that a patient should be treated for pulmonary sarcoidosis. What is your initial starting medication? (n = 36)

Corticosteroids	33, 92%
Methotrexate	0
Azathioprine	0
Other (i-steroids, combination)	0

A Delphi Consensus Study

Sarcoid experts don't always agree!

Question #2: For question 1, what is your initial daily dose (if you selected corticosteroids, use prednisone- equivalent dosing; if you selected a drug that you do not dose daily then specify the frequency of dosing)? (n = 36)

40mg	10, 28%
20mg	9, 25%
1mg	3, 8%
0.5-1mg/kg	1, 3%
1.5-2 mg/kg	1, 3%

A Delphi Consensus Study

Sarcoid experts don't always agree!

Question #6: The second-line agent that I add to corticosteroids or replace corticosteroids with in patients with sarcoidosis who have an inadequate response to corticosteroids is: (n = 36)

Methotrexate	24, 67%
Azathioprine	6, 17%
Hydroxychloroquine	2, 6%
Infliximab	1, 3%
Leflunomide	0

Leflunamide would be my second choice in patients who fail or are intolerant to methotrexate on the available evidence and personal experience. Obviously my opinion was not sought in this study...

Sarcoidosis therapy

Chest X-ray stage 0/1- no active organ disease

No symptoms

No systemic therapy

Highest of research evidence

(+A)

Pietinalho A. Eur Respir J 1996;9:406s

Sarcoidosis therapy

Chest X-ray stage 2-4

Symptomatic or active organ disease

Treat with corticosteroids (A+)

Initial dosing 20-40 mg prednisone (B)

Treat for 12-24 months (D-)

Gibson GJ Thorax 1996;51:238-247

Pietinalho A. Eur Respir J 1996;9:406s

McKinzie BP. Am J Med Sci 2010; 339:1-4

Johns CJ. Medicine 1999;78:65-111

Sarcoidosis Therapy: steroid-sparing agents for chronic sarcoidosis

Methotrexate dose 5-15 mg once a week (A+)

Folic Acid 1 mg/d to reduce toxicity (B)

Baughman RP. Sarcoidosis. Vasc Diffuse Lung Dis. 2000;17:60-66

Lower EE. Arch Intern Med. 1995; 155:846

Vucini VM. Curr Opin Pulm Med. 2002;8:470-6

Sarcoidosis Therapy: steroid-sparing agents for chronic sarcoidosis

Azathioprine 50-200 mg daily
(B+)

Leflunamide 10-20mg daily
(A-)

Mycophenolate 1-3 grams/day
(C-)

Muller-Querheim. Eur Resp J. 1999;14:1117-1122

Lewis SJ. Sarcoidosis Vasc Diffuse Lung Dis. 1999;16:87-92

Morgan SL. Ann Intern Med. 1994;121:833-841

Baughman RP. Sarcoidosis Vasc Diffuse Lung Dis. 2004;21:43-8

Moravan M. Neurology. 2009;72:337-340

Kouba DJ. Br J Dermatol 2003;148:147-148

Moudgil A. Pediatr Nephrol 2006;21:281-285

Treatment of refractory sarcoidosis

Infliximab (Remicade) I.V. 3-5 mg initially, 2 wks,
then q monthly

(A+)

Baughman RP. Am J Respir Crit Care Med.2006;174:795-802

Rossmann MD Sarcoidosis Vasc Diffuse Lung Dis.2006;23:201-208