Introduction
Ankylosing Spondylitis (AS) is a chronic inflammatory disease of unknown aetiology, characterised by sacroiliitis and spondylitis. It typically affects the spine, but other joints and organs are sometimes involved, especially the hips. AS can be a severe disease and lead to serious disability.

Medication, physical therapy and exercise are the main stays of treatment.

For a long period of time, non-steroidal anti-inflammatory drug (NSAID) was the only available option for symptom alleviation in AS. In recent years, however, considerable progress has been made in the pharmacotherapy of AS. Anti-Tumour Necrosis Factor (anti-TNF) agents had been shown to be highly effective in controlling disease activity. Other medications that may be useful include sulphasalazine, methotrexate, pamidronate, thalidomide and intraarticular steroid.

Nonsteroidal Anti-inflammatory Drugs (NSAID)

NSAIDs are effective in control of pain and stiffness in AS patients. Indomethacin was once thought to be more effective than the other NSAIDs. It is necessary to give the maximum dose of 150mg to 200 mg per day in divided doses. Incidence of side effects such as headache, gastrointestinal upset and fluid retention are common. One recent trial showed indomethacin and aceclofenac were equally effective. Perhaps most NSAIDs in adequate doses are equipotent. Different NSAIDs may work best for different individual patients.

To assess the usefulness of a NSAID, it should be given at a sustained dose on a regular basis for about two weeks. After the maximum effect has been observed, further use may be as needed for symptom control.

A recent study showed AS patients who were continuously on NSAID were half as likely to develop radiological progression when compared to those who used NSAID on as needed basis. This made a suggestion for continuous use of NSAID, regardless of the symptom control. More large scale studies are needed to confirm this observation.

COX2 inhibitors had been shown to be useful in double blind controlled trials. Celecoxib 100 mg BD was found to be more effective than placebo. Etoricoxib (90 mg/ day or 120 mg/ day) was also found to be effective. Actually, etoricoxib at this dose had been shown to be more efficacious than naproxen 500 mg BD. Increase in cardiovascular risk is a concern when COX2 inhibitor is used for prolonged period of time though the actual number of serious adverse cardiovascular events was small.

Tumour Necrosis Factor Alpha Antagonists

Etanercept, infliximab and adalimumab are anti-TNF agents that are commercially available. Both etanercept (25mg sc twice weekly) and infliximab (5 mg/ kg infusion at week 0, 2, 6, 12, 18) had been shown to be very effective in AS in double blind placebo controlled studies. Results of adalimumab trials are expected to be published soon. Preliminary data suggest anti-TNF agents can reverse bone marrow changes shown on magnetic resonance imaging (MRI) and prevent progression of radiological spinal changes as well. However, potential side effects such as the increased risk of pyogenic infections, reactivation of latent tuberculosis and rarely development of lymphoma, should be considered when using these agents.

The very high cost of anti-TNF therapy is a major impediment to their widespread use and different countries have different guidelines for its usage.

To put AS patient on anti-TNF therapy, they should meet the following criteria:

1. Firm clinical diagnosis of AS
2. Active disease
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is one common tool used by rheumatologists to assess the disease activity of AS patients.
3. Exclusion of contraindications
   • Active infections
   • Untreated latent tuberculosis
   • Demyelinating disease (eg. Multiple sclerosis, optic neuritis )
   • Heart failure
   • Pregnancy and breast feeding

AS response rate to an anti-TNF agent is up to 80 percent and the response is typically rapid, usually within six weeks of treatment. Positive predictors of response to TNF blockade include

• Young age
• Shorter disease duration
• Good functional status, as measured by the Bath Ankylosing Spondylitis Functional Index (BASFI)
• Elevated ESR and C-reactive protein
Sulphasalazine

There had been many trials on the usefulness of sulphasalazine (SSZ) in AS. The trial with the largest sample and that with the longest treatment duration produced similar results. SSZ had benefit in subset of AS patients with peripheral arthritis. Across all AS patients, SSZ demonstrated some benefits in reducing ESR and easing morning stiffness, but no significant improvement in physical function, pain, spinal mobility, enthesitis, patient and physician global assessment. The literature concluded that patients at early disease stage, with high level of ESR (or active disease) and peripheral arthritis might benefit from SSZ but not those with only symptoms and signs of axial disease.

Methotrexate

Methotrexate (MTX) is one of the most widely used disease modifying anti-rheumatic drugs in the treatment of Rheumatoid Arthritis. However, there is uncertainty in its usefulness for treating AS.

A 2004 systematic review of the effectiveness of MTX in AS found no evidence of benefit. However only two studies met criteria for inclusion and these studies used relative small doses of MTX (7.5 and 10 mg weekly respectively). Furthermore, there were only a total of 81 patients in these two studies. More well designed randomised controlled trials with sufficient patient number and study duration, perhaps with higher dosage regime as well, are needed to establish the role of MTX in the treatment of AS.

Pamidronate

Because of some evidence of anti-inflammatory activity, pamidronate has been evaluated in the treatment of AS. In a double blind RCT, 84 patients with active AS despite NSAIDs were randomised to pamidronate infusion 60mg monthly or 10 mg monthly each for a period of 6 months. The decrease in BASDAI was significantly greater with the higher dose therapy. Pamidronate appears to be an option when other medications are not feasible or useful.

Thalidomide

One abstract reported an open study of thalidomide (200-300 mg per day) in 30 patients. After one year, 80 % of patients had improved more than 20 % in 4 of 7 clinical outcome measures (BASFI, BASDAI, early morning stiffness, total body pain score, spinal pain, patient global and physician global assessment). Well defined, controlled studies are needed to define the role of thalidomide in the treatment of AS. The cutaneous and neurological adverse effects are of concern in its long term usage.

Steroid

Long-term systemic steroid is not recommended for AS patient. Intraarticular steroid for peripheral arthritis and local injection to painful plantar fasciitis can be helpful. Injection of long acting steroid to sacroiliac joint may be beneficial to patients unresponsive to other measures.

Physical therapy and exercise

It has been demonstrated that supervised group and individual physical therapy can lead to symptomatic relief and significant improvement and maintenance of spinal mobility. An initial evaluation and treatment by physical therapist should be part of every therapeutic regimen. Physical therapy involves postural training, range of motion exercises, and hydrotherapy. All AS patients should be advised on regular specific home exercises. In addition, pain relief measures such as local heat or cold can be tried.

Conclusion

Recent advances in our understanding of ankylosing spondylitis and the availability of potent therapeutic options call forth a change from the traditional approach to the management of the disease. Primary care physicians and specialists alike should adopt an expeditious rather than an expectant approach in the diagnosis, referral and treatment of patients suffering from ankylosing spondylitis in order to prevent irreversible functional disability.