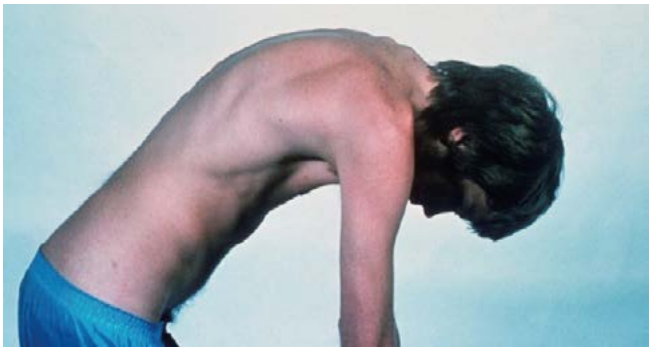
What is ankylosing spondylitis?

Ankylosing spondylitis (AS) is a painful, progressively debilitating inflammatory disease, the main symptom of which is back pain[1]. AS occurs in approximately 1% of the general population and typically affects young men and women aged 25 or older[2,3], with two to three times more men affected than women[1].

AS is part of a family of long-term inflammatory diseases called spondyloarthropathies that also includes psoriatic arthritis (PsA)[4]. The causes of AS are not clearly understood but genetic factors seem to be involved[2,5]. The HLA-B27 gene is associated with a significantly increased risk of developing AS and family members of those with AS are at higher risk of developing the condition[5-7].

AS causes high levels of disability

AS usually has a serious impact on movement in the spine, which affects a person's physical functioning and impacts quality of life[1]. Up to 70% of patients who go on to develop severe AS will form spinal fusions (where the bones grow together) over 10 to 15 years, which significantly reduces mobility[8]. Chronic fatigue and sleeplessness are also features of AS[2].



Spine damage in ankylosing spondylitis: Outward curvature of the spine due to fusion of the vertebrae in a man with ankylosing spondylitis.

High levels of disability affect people's ability to work and people with AS are 78% more likely to shorten their working hours than people without the condition, limiting their job options[8]. There is a strong association between the physical impact of AS and anxiety and depression[9].

AS is also associated with complications such as[1]:

- Osteoporosis,which occurs in up to half of patients with AS, especially in those whose spine is fused, and it increases the risk of spinal fracture
- Inflammation of the eye, called uveitis: occurs in about 40% of those with spondyloarthritis, and whose symptoms include redness and pain
- Inflammation of the aortic valve, which can occur over time
- Psoriasis, a common, non-contagious inflammatory skin condition characterized by scaly skin
- Intestinal inflammation, which may be severe enough to need treatment

The immune system's role in AS

Interleukin-17A (IL-17A) is one of the many proteins in the body called cytokines that help protect the body against infections[10]. Cytokines usually work by signalling to infection-fighting cells that they need to mount an immune response once foreign invaders, such as bacteria or

other disease causing germs, have been detected[10]. In inflammatory diseases, IL-17A has been identified as playing a key role in disease development[11].

Higher concentrations of IL-17A have been found in areas surrounding the bones and joints in people suffering from AS, particularly in the fluid and lining of the joints[12-14].

- IL-17A acts as signal to infection-fighting cells, triggering an inflammatory response that results in bone erosion and new bone formation to replace lost elastic tissue in areas surrounding the bones and joints[10].
- Infection fighting cells release IL-17A, causing inflammation and new bone formation[10].

Treatment goals in AS: preventing disability

The long-term consequences of AS are linked to the structural damage and functional loss caused by the disease, which are permanent[4]. The goals, therefore, of management are to maximise long-term health-related quality of life by reducing patients' levels of pain, improving physical function relative to activities of daily living and work performance, reducing disability, and preventing further deterioration[4,15].

Unmet treatment needs in AS

Patients with AS have very few treatment options available to them[4]. For patients who do not respond to non-steroidal anti-inflammatory drugs (NSAIDS), anti-TNF (tumor-necrosis-factor) medicines are the current standard of care, but are not effective for all patients[4]. Approximately 20-40% of patients fail to achieve sufficient clinical improvement on anti-TNFs[4].

Newer, innovative treatments that specifically target the cytokines that trigger inflammation, such as IL-17A, interrupting the inflammatory cycle in AS have been developed in response to this unmet need. These treatments have shown positive results in the treatment and management of AS[16].

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