

# Autoimmunity, Osteoporosis and Vitamin D



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## Abstract

Autoimmune diseases may be accompanied by osteoporosis. Rheumatoid arthritis is accompanied by periarticular and systemic osteoporosis. Ankylosing spondylitis is accompanied by bone formation in the spine and the surrounding tissues. However, this process is also accompanied by severe osteoporosis which occurs early in the process of the disease. Systemic lupus erythematosus is also accompanied by osteoporosis and increased risk for fractures. Inflammatory bowel disease is a systemic autoimmune disease which is associated with inflammatory process in the bowel and is accompanied by severe vitamin D deficiency and osteoporosis. Osteoporosis in these diseases is due to systemic inflammation and the process of autoimmunity. During the process of autoimmunity inflammatory cytokines are secreted which impact bone metabolism. In particular, interleukin-6 and TNF $\alpha$  are secreted during the autoimmunity process. These inflammatory cytokines induce osteoclastogenesis and increased bone resorption. Thus, the systemic process of autoimmunity is accompanied by osteoporosis. Vitamin D is a secosteroid hormone which is involved in bone metabolism. It induces calcium absorption from the intestine and thus it promotes bone mineralization. Vitamin D is also involved in the regulation of the immune process with multiple effects. It enhances the immune response to bacteria and viruses and is thought to induce immune tolerance. Thus, vitamin D deficiency may be related to the development of autoimmune diseases. In conclusion, vitamin D may prevent autoimmune diseases and may regulate and optimize bone metabolism in the context of autoimmune diseases.

**Keywords:** Autoimmunity; Osteoporosis; Vitamin D; Vitamin D deficiency; Rheumatoid arthritis; Ankylosing spondylitis

## Introduction

Autoimmune diseases have been found to be related to an increased risk for the development of osteoporosis [1-3] (Figure 1). Rheumatoid arthritis (RA) is known to be associated with periarticular osteoporosis and systemic osteoporosis [1,4]. Periarticular osteoporosis in the context of RA accompanies the inflammatory process in the synovium and is known to be associated with the severity and the progression of the disease [5]. Ankylosing spondylitis (AS) is an autoimmune disease in which involvement of the entheses is observed [6]. The disease is characterized by bone formation around the spine [7]. However, simultaneously it is characterized by severe osteoporosis [8,9]. It has been suggested that male osteoporosis with a fracture may suggest that the patient should be screened for AS [10]. Systemic lupus erythematosus (SLE) is also characterized by an increased risk for the development of fractures [11]. Inflammatory bowel disease (IBS) is also accompanied by osteoporosis [12,13].

Systemic inflammation and the systemic autoimmune process in these diseases leads to secretion of inflammatory cytokines such as TNF $\alpha$  and IL-6 [14]. These inflammatory cytokines impact bone metabolism [15]. They induce osteoclastogenesis [16] and thus may enhance bone resorption [17] and lead to the development of osteoporosis [18,19].

Vitamin D deficiency may be related to the development of autoimmune diseases [20,21]. Vitamin D deficiency may be related to an increased risk for the development of RA [22-24]. Vitamin D deficiency is also observed in SLE [25-27]. Vitamin D deficiency is also observed in IBS [28]. Vitamin D may protect from the development of autoimmune diseases [29,30]. Vitamin D may also protect from the development of osteoporosis and may serve in the management of osteoporosis in the context of autoimmune diseases [29].

### Vitamin D and Autoimmunity

Vitamin D is a secosteroid hormone [31]. It regulates bone metabolism and is involved in the regulation of muscle function [32]. It induces intestinal calcium absorption and promotes bone mineralization. Vitamin D deficiency leads to osteomalacia and as

it induces secondary hyperparathyroidism it leads to increased bone resorption and may be involved in the development of osteoporosis [33]. Vitamin D enhances immune function and induces immune tolerance [20,34]. Therefore, vitamin D deficiency may be related to the development of autoimmune diseases [30] (Figure 2).

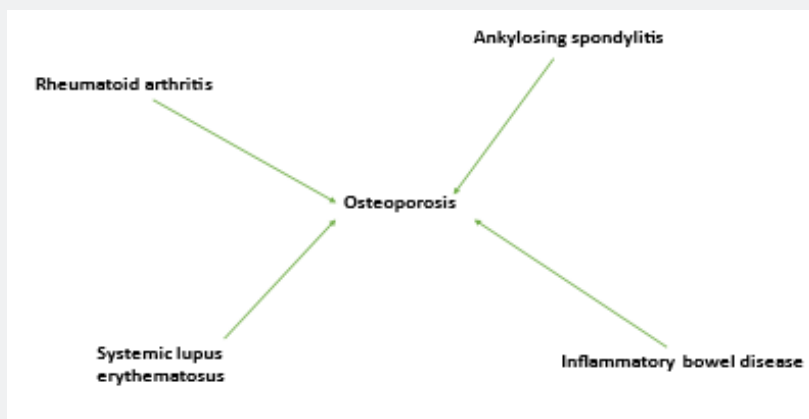


Figure 1: Autoimmune diseases characterized by an increased risk for the development of osteoporosis.

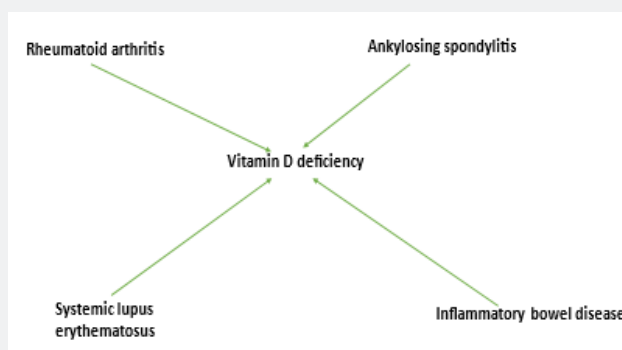


Figure 2: Autoimmune diseases characterized by vitamin D deficiency.

### Rheumatoid Arthritis

The risk for the development of RA is increased in the presence of vitamin D deficiency [22,24,35,36]. In addition, RA is accompanied by vitamin D deficiency and RA activity is related to vitamin D deficiency, i.e. RA is severe in the presence of vitamin D deficiency [4].

### Ankylosing Spondylitis

Ankylosing spondylitis is a systemic autoimmune disease affecting the entheses [37]. It is accompanied by bone formation [6]. However, in the presence of bone formation bone resorption is paradoxically increased and leads to osteoporosis and fractures [9]. Fracture in a young male patient may be an indication for investigation for the presence of AS [10]. In AS fractures may lead

to neurological complications and disability [38]. AS seems to be accompanied by vitamin D deficiency, which may be related to disease activity [39].

### Systemic Lupus Erythematosus

SLE is the prototype of the multiorgan systemic autoimmune diseases [40]. It preferentially affects women in the reproductive age. It runs a variable course from very mild to severe disease with multiorgan involvement which may lead to death. Renal involvement may be observed in SLE and may lead to renal insufficiency. Severe infections may be observed during SLE and may be a presenting event. Sun exposure may induce disease exacerbation [41]. Thus, patients are advised to avoid sun exposure. As a result, vitamin D deficiency is present in patients with SLE and may be related to disease severity [25-

27]. SLE patients have an increased risk for the development of osteoporosis and fractures [42,43].

### Inflammatory bowel disease

Inflammatory bowel disease (IBD), Crohn's disease and ulcerative colitis, is a group of systemic autoimmune diseases affecting multiple organ systems. It is characterized by various manifestations, including abdominal pain and bowel movement abnormalities. Vitamin D deficiency has been observed in patients with IBS [44]. Vitamin D administration may have beneficial effects in IBD patients, as far as osteopenia, depression and protection

### Protective role of vitamin D on bone metabolism

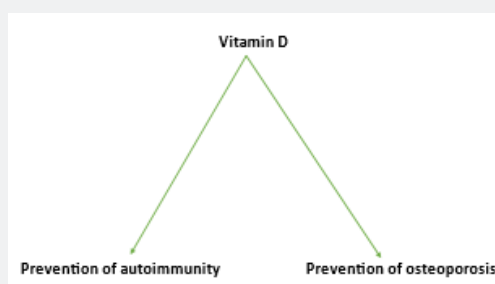


Figure 3: The role of vitamin D in autoimmune diseases.

Vitamin D regulates bone metabolism. It induces bone mineralization. Therefore, vitamin D supplementation may improve bone metabolism, improve osteopenia and osteoporosis [49-51] (Figure 3). Additionally, vitamin D may improve muscle function and protect from the development of sarcopenia.

### Conclusion

Autoimmune diseases are characterized by an increased risk for the development of osteoporosis. In addition, autoimmune diseases seem to be accompanied by vitamin D deficiency. The autoimmune process seems to be related to the development of osteoporosis, as inflammatory cytokines are secreted which affect bone metabolism. Vitamin D is an immunomodulatory hormone and may play a protective role in the prevention of autoimmunity. Vitamin D may be beneficial in autoimmune diseases by protecting from the autoimmune process and by exerting a beneficial role on bone metabolism and preventing osteopenia and osteoporosis.

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from colorectal neoplasia is concerned [45].

### The role of vitamin D in autoimmune diseases

#### Protective role of vitamin D from autoimmunity

As already discussed, vitamin D deficiency may be related to an increased risk for the development of RA. Vitamin D deficiency may also be related to an increased risk for the development of multiple sclerosis. Vitamin D supplementation may therefore exert a protective role as far as prevention from the development of autoimmunity is concerned [46-48].

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