



Risk of infection with Anti-Tumor Necrosis Factor Therapy?

Background: Tumor necrosis factor (TNF) antagonists have demonstrated effectiveness in reducing activity and progression of chronic inflammatory conditions such as rheumatoid arthritis and Crohn's disease.^{1,2} TNF, however, plays an important role in the body's defense against infection particularly intracellular infections such as tuberculosis (TB)³; therefore anti-TNF therapy may increase patients' susceptibility to infections.³ The three TNF antagonists currently available in Canada are infliximab, adalimumab (both monoclonal antibodies that bind irreversibly to TNF) and etanercept (a soluble TNF receptor that forms a short-lived reversible bond with TNF).^{3,4}

Response: Although many of the earlier studies did not report an increased risk of infection, results from a recent meta-analysis of randomized controlled trials⁵, prospective cohort studies^{6,7} and post-marketing adverse event reporting programmes^{8,9} suggest the following:

- **Anti-TNF therapy approximately doubles the risk of serious infection.**
- **Patients using infliximab or adalimumab are at least three times more likely than those on etanercept to develop TB and other granulomatous infections (probably due to the difference in mechanisms).**
- **The number needed to harm (infliximab or adalimumab) is 59, i.e., one additional serious infection for every 59 patients treated for 3 – 12 months.**
- **The actual incidence of infection reported in studies was between 5 and 6 percent.**

Important Points:

- Patients requiring anti-TNF therapy have a higher baseline risk of infection (active or severe disease processes, disabilities caused by the disease, concurrent immunosuppressant therapy).¹⁰ **Patients need to be aware that anti-TNF therapy increases the risk of serious infection, of the signs and symptoms of infection (fever, malaise, night sweats, cough, unexplained weight loss), and of the importance of reporting these to their physician as soon as possible.**^{10,11}
- **If an infection occurs, anti-TNF therapy should be discontinued until the infection is resolved.**¹⁰
- The infection most frequently associated with anti-TNF therapy is TB. It is thought to be primarily due to reactivation of latent infection rather than new infection.¹² **Ensure patients have been screened for exposure risk and latent TB (PPD test, chest x-ray).¹ Monitor for TB especially during the first 12 months of therapy even if tests are negative.**^{10,12}
- Patients on anti-TNF therapy are also at higher risk from foodborne disease such as *Listeria monocytogenes*, and *Salmonella* species.^{10,12} **Patients should be advised on the importance of proper food handling and avoidance of potentially infected foods (unpasteurized milk products, undercooked meals and read-to-eat meals).**^{10,12}

- **Consider recommending pneumococcal vaccination before initiation of anti-TNF therapy.**¹⁰ Cases of fatal pneumococcal sepsis and necrotizing fasciitis have been reported.¹⁰

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