

# Yellow fever vaccine used in a psoriatic arthritis patient treated with methotrexate: a case report

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## Abstract

The yellow fever vaccines on the market are contraindicated for immunocompromised and elderly patients. A case of yellow fever vaccine used in a 27-year-old Slovenian male with psoriatic arthritis during treatment with methotrexate is described. We demonstrate a positive case, since there were no adverse effects in concurrent administration of yellow fever vaccine and methotrexate. This patient did not show severe adverse reactions and did not contract yellow fever despite potential exposure. More research is needed on possible adverse effects of concurrent administration of yellow fever vaccine and methotrexate to determine the potential of this method for more frequent use.

**Keywords:** yellow fever vaccine, methotrexate, immunocompromised patients, case report

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## Introduction

Yellow fever (YF) is a vector-borne disease affecting humans and non-human primates in tropical areas of Africa and South America (1). The causative Flavivirus is endemic in parts of tropical Africa and South America and is transmitted to humans and primates by mosquitoes. The chance that an unvaccinated traveler to West Africa will die of yellow fever is estimated at 1:650 to 1:5,000 visitors per month of stay, depending on whether an epidemic occurs (2). The incidence of YF was dramatically reduced following the development of live attenuated vaccines in the 1930s (3). The vaccines on the market are contraindicated for immunocompromised and elderly patients (4). The only manner of preventing YF infection is by means of vaccination, and the protection rate is at least 92% (5). Because of the high mobility of people and workers from all over the world to areas of South America and Africa, it is necessary to know about using YF vaccine as a last resort in immunocompromised patients.

A PubMed search was conducted using the terms YF and methotrexate (MTX) to identify randomized controlled trials and case reports that evaluated this effect for such patients. This paper describes a case of YF vaccination in a middle-aged Slovenian tour guide with psoriatic arthritis (PA).

## Case report

A 27-year-old Slovenian male was admitted to an outpatient clinic in April 2011 because of polyarthritis. In his medical history he had no history of liver disease, seizures, lupus, cancer, or rheumatic arthritis. He was not addicted to alcohol or other drugs. Baseline laboratory results collected at admission included a normal complete blood cell count, normal liver enzymes, and normal liver function tests. C-reactive protein (S-CRP) was 48 mg/L (normal < 5 mg/L) and erythrocyte sedimentation rate (ESR) was 20 mm/h (normal < 15 mm/h). Alkaline phosphatase, bilirubin, albumin, and prothrombin time were within the normal range. Auto-immune hepatitis markers and thyroid tests were normal and HIV infection was excluded. He was diagnosed with PA according to Moll and Wright criteria, and sulfasalazine (2,000 mg daily) was

introduced. His medication prior to hospitalization included only paracetamol (500 mg daily).

After 2 months, sulfasalazine was withdrawn due to lack of effectiveness and therefore switching to MTX (10 mg per total body surface weekly) was necessary. Folic acid (2.5 mg daily) was added to MTX therapy. The MTX dosage was titrated up to 20 mg weekly over 4 weeks. Before switching to MTX, laboratory results excluding S-CRP and ESR rate were normal. After adjustment of the optimal dosage of MTX, S-CRP level, ESR, and joint pain declined progressively over 2 months. In the 3rd month of treatment with MTX, the patient requested primary vaccination because of his profession. He is a tour leader in South America. Two months before the vaccine was introduced, MTX was discontinued. A single dose of 0.5 ml of reconstituted Stamaril(R) 48 vaccine from the manufacturer Sanofi Pasteur was delivered in intramuscular injection form into the right arm. A pain diary form was completed and temperatures prior to and after vaccination were measured to provide information on possible exacerbation of the underlying arthritis and vaccine reactions. There were no adverse events after vaccination. Adverse effects were monitored for 3 months. The dosage of MTX was titrated up to 20 mg weekly again over 8 weeks and then titrated down slowly.

One year after vaccination, the patient is receiving a 10 mg weekly dosage of MTX and his PA is controlled. He often goes to South America. Again, no symptoms of infection with YF have been observed. Serological examination for neutralizing antibodies against the YF virus vaccine strain were performed and were within the normal range. Laboratory results were taken after vaccination and every 2 weeks in treatment with MTX, and there were no deviations.

## Discussion

We were only able to find three studies or manuscripts on MEDLINE on the topic of YF vaccine and MTX. The first study was performed in 2009 in Brazil. Forty-two patients that received YF vaccination during treatment with MTX were described. Eight out of 42 patients that received YF vaccination during treatment with MTX had adverse events ranging from myalgia to elevated liver

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enzymes. One patient also received infliximab, and two others cyclophosphamide. None of the patients had developed severe neurologic or visceral disease (6). It is not clear from this paper how many patients were vaccinated for the first time. Antibody levels after vaccination were not determined. A 2011 study stated that primary vaccination with live attenuated vaccines in patients receiving TNF antagonists should be avoided at all times (7). There are some possible alternatives to YF vaccination in patients that have received MTX. Exemption certificates for patients that travel inside safe areas within countries where YF is endemic is the first option. Another option is pausing immunosuppressive treatment when possible. A third option is to measure the level of neutralizing antibodies in patients that have previously been vaccinated because protective antibody levels may persist up to 30 to 35 years (8).

Recommendations for vaccination in patients with autoimmune inflammatory rheumatic diseases based on the currently available evidence and expert opinions were formulated by EULAR. More research is needed, particularly regarding the incidence of vaccine-preventable infectious diseases and the safety of vaccination in patients with autoimmune inflammatory rheumatic diseases. Current guidelines for patients using low-dose MTX are not so strict that live-

attenuated vaccines should be withheld at all costs (9). However it is necessary to control symptoms of PA during the vaccine administration period. Serological examination for neutralizing antibodies against the yellow fever virus vaccine strain after vaccination of immunocompromised patients should be encouraged to document efficacy.

### Conclusion

For our patient, YF vaccination was the appropriate approach. The live-attenuated YF vaccine in a patient using MTX did not induce severe adverse events. The patient did not contract yellow fever despite possible exposure to the virus. Current guidelines for patients using low-dose MTX do not state that live-attenuated vaccines should be withheld at all costs. This case report may serve to help clinicians and clinical pharmacists when treating immunocompromised patients as it clearly demonstrates no adverse events after vaccination. More research is needed on the safety and efficacy of YF vaccination in rheumatic patients treated with MTX and other immunosuppressive drugs.

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