

# Red Man Syndrome: Beyond the story of Mississippi mud

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**Abstract:** Antibiotic therapy is not free of side effects. Some of them appear within few minutes after administration which may be IgE- dependent or not, but can put the patient and treating physician in trouble, even for a short time. Red Man Syndrome (RMS) is a rare side effects of some antibiotics, particularly vancomycin. In this brief review we will explain the pathophysiology and recommendation about its treatment and prevention and also describe other less reported antibiotics which can cause this syndrome.

**Keywords:** Antibiotic, Side effect, Red Man Syndrome (RMS), Vancomycin.

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**Vancomycin** was discovered in 1952 and its Initial preparations were not purified and brown. Thus, vancomycin named as "Mississippi mud." At that time, physicians thought Red man syndrome (RMS) was related to its impurities. However, even after purification, RMS continued to be reported. (1)

"Red man syndrome" or "Red neck syndrome" is generally related to rapid infusion of the first dose of the vancomycin but there are reports of its occurrence even following slower infusion rates or after several days of transfusion. (2,3) Discontinuation of the vancomycin infusion and administration of an antihistamine subsides the reaction. RMS often develops with intravenous vancomycin but rarely occur after oral (4-7), intraperitoneal (8) or local (9) vancomycin administration. RMS usually begins 4 to 10 minutes after the starting the first dose of intravenous vancomycin. RMS occurs in 4% to 50% of infected patients treated with intravenous vancomycin. (2,10) Patients under 40 years of age are at greatest risk of severe RMS reactions. (2,11)

vancomycin activates the degranulation of mast cells and basophils increasing histamine release in a non-IgE mediated process. The amount of histamine release correlates to the dose and the rate of vancomycin infusion. (2,12)

RMS primarily is a pruritic, erythematous rash on face, neck, and upper torso, which may also involve the extremities to a lesser degree. Severe reactions include angioedema, hypotension, tachycardia, and chest or back pain. RMS usually is mild and easily managed. However, there are rare cases of life-threatening RMS reactions. (2,3) The diagnosis of RMS is on clinical basis, but, Severe cases should be differentiated from IgE-mediated anaphylactic reactions. (3) Both RMS and anaphylactic reactions have similar findings. (13,14)

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Minor symptoms can be managed with antihistamines. Most episodes will resolve within 15-20 minutes. Severe cases should be evaluated for anaphylaxis. If, it was ruled out, then antihistamines such as diphenhydramine and ranitidine can both be started intravenously. Normal saline intravenous boluses are used to treat hypotension. If alternative antibiotics to vancomycin are available, better to be used. If vancomycin must be continued, patients should be received premedication with diphenhydramine and ranitidine 1 hour before each dose, and vancomycin should be administered over 2-4 hours under close monitoring. (13,14)

There are also case reports of RMS related to other antibiotics such as rifampin (15-19), cefepime (20), teicoplanin (21-23), ciprofloxacin (24) and amphotericin B. (25) Like vancomycin, they are capable of causing direct degranulation of mast cells and basophils. It is unknown whether it can be prevented with slower cefepime infusion and pre-infusion antihistamines, as is the case with vancomycin. On the other hand, most cases of rifampin-associated RMS were following its overdose, not in regular doses uses in tuberculosis treatment. Basically, RMS is extremely uncommon with teicoplanin use, but due to probability of cross-reactivity between teicoplanin and vancomycin, the former is not a good alternative in cases of vancomycin-associated RMS.

*In conclusion*, healthcare providers should be made aware of the presentation of red man syndrome as well as the management of this condition to improve patient outcomes. Patients should be provided with the most appropriate care and educated on the condition.

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