

# Prozone phenomenon in secondary syphilis

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## Abstract

Prozone phenomenon is a false negative response resulting from high antibody titer which interferes with formation of antigen- antibody lattice, necessary to visualize a positive flocculation test. We present a case of secondary syphilis who presented to us with features of contact irritant dermatitis. She initially tested non- reactive for VDRL testing but tested positive with higher dilution. The prozone phenomenon is attaining importance because of increasing prevalence of Acquired immune deficiency syndrome. So one needs to be familiar with the occurrence of prozone phenomenon.

**Key words:** Acquired immune deficiency syndrome, flocculation test, prozone phenomenon, syphilis

## INTRODUCTION

The prozone phenomenon refers to a false negative response resulting from overwhelming antibody titers. The prozone effect is most often associated with secondary syphilis, Human immunodeficiency virus (HIV) co-infection, and pregnancy.<sup>[1]</sup> Published reports document the incidence of prozone phenomenon to be between 0.2 and 2%. This is believed to be higher in the HIV population.<sup>[2]</sup>

The incidence of the prozone phenomenon is attaining clinical significance due to increasing population at risk for sexually transmitted diseases, especially those who are HIV positive.

We describe the occurrence of the prozone phenomenon in a patient with secondary syphilis.

## CASE REPORT

A 36-year-old female presented with a chief complaint of rash all over the body, of 15 days duration, associated with severe itching. On detailed history elicitation, the patient stated that the rash was asymptomatic to begin with. It started on the right forearm, and later became generalized. The patient applied some native medications and developed generalized itching and presented with a picture of contact irritant dermatitis in the form of papules, vesicles, and scaling, all over the body. The patient was treated for the same with a combination of topical steroids and antihistamines. The patient had little symptomatic relief with this. The patient's rash was persistent in the form of macules, papules, and scaling. A thorough examination revealed the presence of few lesions on the genitalia mainly on the labia majora [Figure 1a], which were flat topped papules and the patient also had a mucous patch over the hard palate [Figure 2a]. Thus, secondary syphilis was strongly suspected and the patient was subjected for Venereal Disease Research Laboratory (VDRL) testing. The VDRL testing was non-reactive. As the suspicion of secondary syphilis was high, we conducted a detailed examination of the patient's husband. He denied a history of any sexual exposure and any genital lesion, but gave a

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Figure 1a: Genital lesions — Before treatment



Figure 1b: Disappearance of lesions after treatment



Figure 2a: Oral lesions — before treatment



Figure 2b: Oral lesions — after treatment

history of intermittent urethral discharge. The rest of the physical examination was found to be within normal limits. He was also tested for VDRL and was found to be positive. Therefore, we requested for repeat VDRL test, with higher dilution and it was reactive with 1 : 512 dilution. The patient and husband were subjected to HIV testing, and both were found to be seropositive. The patient was given 2.4 MU of Benzathine penicillin. The patient started to show improvement within 48 hours. Both husband and wife were treated. All skin, oral [Figure 2b] lesions regressed and condyloma lesions [Figure 1b] disappeared after one month of follow-up. The patients were referred to the Voluntary Counseling and Testing Center (VCTC) for further evaluation and initiation of Antiretroviral therapy.

## DISCUSSION

Prozone phenomenon is an immunological event, relying on an antigen–antibody interaction such as in rapid plasma reagin (RPR) or VDRL.<sup>[3]</sup> An

agglutination or precipitation reaction will be positive (i.e., visible through lattice formation) depending on several factors that determine the size and solubility of the immune complex formed *in vitro*. The optimal ratio of the antigen antibody yields an insoluble precipitate that is visible, thus rendering the test positive.<sup>[4]</sup>

The zone of equivalence defines this optimal ratio. In the zone of the antibody excess (prozone) or antigen excess (post zone), false negative results will occur.<sup>[4]</sup>

The prozone phenomenon in the setting of syphilis may become prevalent because of the current acquired immunodeficiency syndrome (AIDS) epidemic.<sup>[2]</sup> As syphilis and HIV mutually increase the chance of contracting other diseases, anomalous B-cell behavior can lead to hyper-responsiveness to antigenic stimulation, leading to excess antibody production.<sup>[5]</sup>

Many hospital laboratories do not routinely test for the prozone phenomenon. This is performed by diluting the patient's serum to bring the antibody concentration into the zone of equivalence. Therefore, it is important to notify the laboratory in this regard, when the clinical findings strongly suggest syphilis and when the nontreponemal serological test results are negative.

## CONCLUSIONS

The purpose of this article is to focus attention on the prozone phenomenon in the setting of syphilis, which may become more prevalent due to increasing HIV incidence. Thus, an astute dermatologist who maintains a high index of suspicion and continued familiarity with protean manifestations of secondary syphilis should look for the prozone phenomenon in suspected cases.

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