



The Clinical Presentation of Syphilis in HIV-Infected Men who have Sex with Men (MSM) in an Urban Clinic

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Abstract

Background: The incidence of syphilis in HIV-infected MSM continues to increase. Rather than being diagnosed at the time of symptom presentation, these cases are often discovered later by routine serologic screening. The aim of this study was to describe the clinical presentations of syphilis in HIV-infected MSM and time to diagnosis and initiation of treatment.

Methods: We conducted a retrospective chart review of all HIV-infected MSM diagnosed with incident syphilis at our HIV clinic from 1/1/00 to 12/31/07. Patients were included if they had a prior documented negative syphilis serology and no history of syphilis. The medical record from the time of the last negative serology to syphilis diagnosis (maximum one year) was reviewed for symptoms of syphilis. Kaplan-Meier and Cox proportional hazard models were used to calculate the predictors of a complete serologic response to treatment.

Results: 118 patients were included: median age of 38 (IQ range 34-43), median CD4 of 399 cells/ μ L (IQ range 307-450), and 66 (56%) with HIV RNA <400 copies/mL. There was a median of 200 days (IQ 135-309) from the prior negative syphilis serology to the diagnostic test. Table 2 shows symptoms occurring in at least 10% of subjects, proportion with a delay in diagnosis from presentation with symptom, and median delay. 54 (46%) had a delay in diagnosis. The median time to negative serology after treatment was 396 days (IQ range 266-1130). Predictors of longer time to negative serology include a higher titer at diagnosis ($p<.001$), late latent syphilis ($p<.001$) and HIV RNA level >400 copies/mL ($p<.1$). Among patients with primary, secondary, or early latent syphilis, one vs. three intramuscular injections of benzathine penicillin G was not associated with the time to negative syphilis serology ($p>.5$). 26 (24%) became re-infected with syphilis.

Conclusions: The presentation of syphilis in HIV-infected MSM was characterized by a wide range of symptoms that were frequently not recognized as syphilis. A higher level of suspicion among providers and more frequent serologic testing of HIV-infected men are warranted.

Methods

- Retrospective chart review of all HIV-infected MSM diagnosed with incident syphilis at our HIV clinic in New York City from 1/1/00 to 12/31/07.
- Subjects included if they had prior documented negative syphilis serology and no history of syphilis.
- Medical record reviewed from time of the last negative serology to syphilis diagnosis (maximum one year) for symptoms of syphilis, stage of diagnosis, treatment, and re-infection.
- Kaplan-Meier and Cox proportional hazard methods used to calculate the predictors of a complete serologic response to treatment.
- Re-infections were defined as a 4-fold increase in RPR titer and documentation of diagnosis and treatment. Subjects were censored at the time of the re-infection for predictors of response.

Table 1:
Subject Characteristics (N=118)

Age at Diagnosis (Years)	Median (IQ range)
HIV RNA <400 copies/mL	38 (34-43)
Race/Ethnicity	
White	56 (52%)
Black, non-Hispanic	39 (33%)
Hispanic	40 (34%)
Other	4 (3%)
CD4 Count	
At syphilis diagnosis	399 (267-509)
Neurosyphilis	213 (114-577)
Syphilis stage at diagnosis	
Primary	8 (7%)
Secondary	80 (68%)
Early Latent	17 (14%)
Late Latent	13 (11%)
RPR titer at diagnosis	
<1:8	20 (17%)
1:8-1:32	42 (36%)
1:64-1:128	44 (37%)
>1:256	12 (10%)

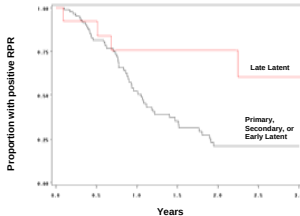
Table 2:
Clinical Presentations and Diagnosis Delays (N=118)

Symptoms (most to least common)	N (%)	N (%) with delay in dx from onset of symptom	Median delay in days
Generalized rash	70 (59%)	16 (23%)	25
Pain in joints and bones	44 (37%)	4 (9%)	7
Sore throat	35 (21%)	14 (59%)	44
Genital chancre	21 (18%)	12 (57%)	56
Subjective fever	13 (11%)	7 (54%)	42
Regional rash	13 (11%)	1 (8%)	38
Chancres	13 (11%)	6 (46%)	73
Mucous chancre	12 (10%)	3 (25%)	78
Asymptomatic + RPR	9 (8%)	-	-

54 (46%) had a delay in diagnosis from onset of any symptom to treatment

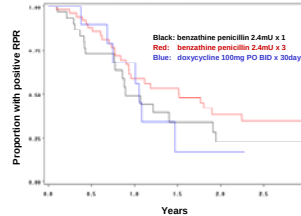
Results

Time to Negative RPR Titer After Initial Treatment by Diagnosis Stage



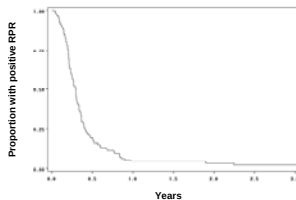
In a multivariate model, higher baseline RPR titer ($P<.001$) and latent syphilis ($P=.001$) were associated with a longer time to negative RPR titer. Detectable HIV-1 RNA was marginally associated ($P=0.1$).

Time to Negative RPR Titer After Initial Treatment by Regimen



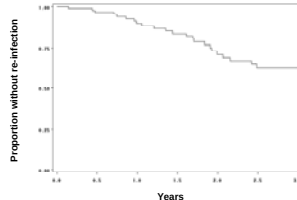
Treatment regimen was not associated with a longer time to negative RPR titer among subjects with primary, secondary, or early latent syphilis.

Time to 4-Fold Decrease in RPR Titer



96% of patients had a 4-fold decrease in RPR titer at one year.

Time to Re-infection After Initial Treatment



The Kaplan-Meier adjusted rates of re-infection at 1, 2 and 3 years after treatment were 10%, 29% and 38%.

Background

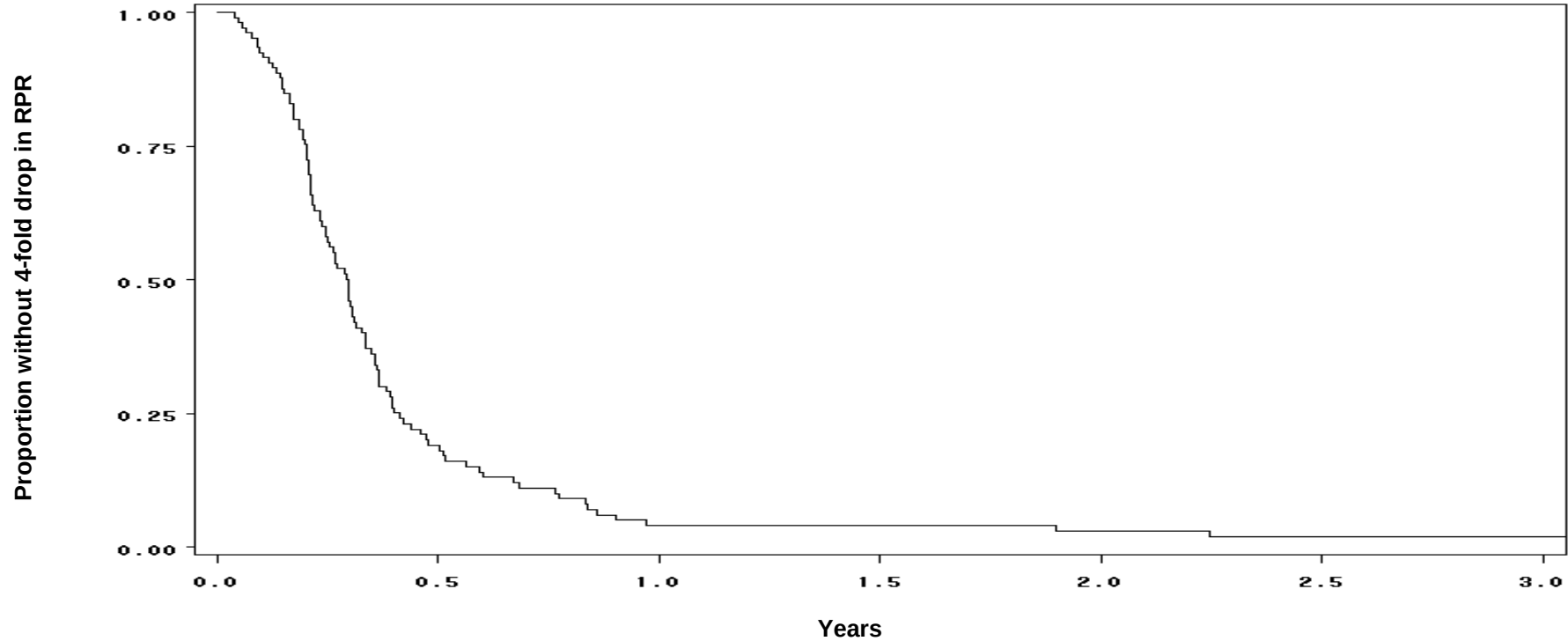
- After a nadir in 2000, the U.S. rate of syphilis has increased, notably among men, from 3.0 per 100,000 in 2001 to 5.7 per 100,000 in 2006.¹
- MSM were 4% of cases in 2000 and approximately 64% in 2006. 60% are HIV-infected, urban MSM.^{1,2}
- In New York City, 97% of syphilis cases are among MSM, half of whom are HIV-infected. The rate of syphilis in NYC doubled in the first quarter of 2007.³
- Rather than being recognized at the time of symptomatic presentation, many cases of early syphilis are discovered later by routine serologic testing.
- The aims of this study were to describe the presentation of syphilis in HIV-infected MSM, time to diagnosis and treatment, RPR response, and re-infection rates.

¹ www.cdc.gov/nchs/data/syphilis.htm
² Bettsman JE. Primary and secondary syphilis among men who have sex with men in the United States, 2004. STD-109, Seattle, WA, 2007 [abstract Q-089].
³ www.nyc.gov/health/doh/html/2007/ty054-07.shtml

Conclusions

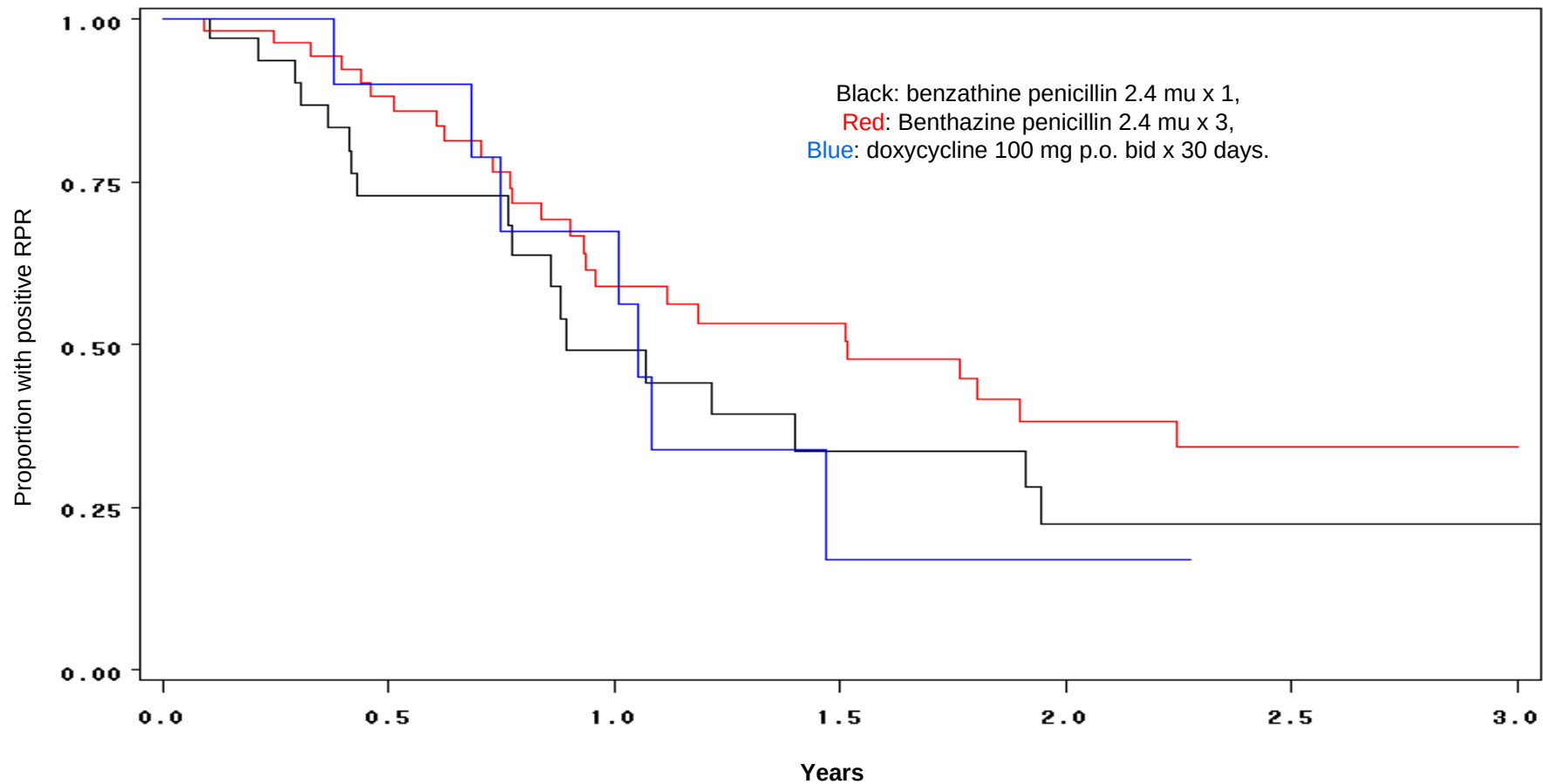
- Syphilis is common in the HIV-infected MSM community
- The presentation of syphilis is characterized by a wide range of symptoms that were frequently not recognized as syphilis including sore throat and cervical lymphadenopathy.
- Late latent syphilis is associated with a prolonged time to serologic response when adjusted for baseline RPR titer. Serologic response is not affected by treatment regimen.
- Re-infection is common with an observed rate of approximately 10% per year.
- A higher level of suspicion among providers and more frequent serologic testing of HIV-infected men are warranted
- Acknowledgements:**
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Time to 4-Fold Decrease in RPR Titer

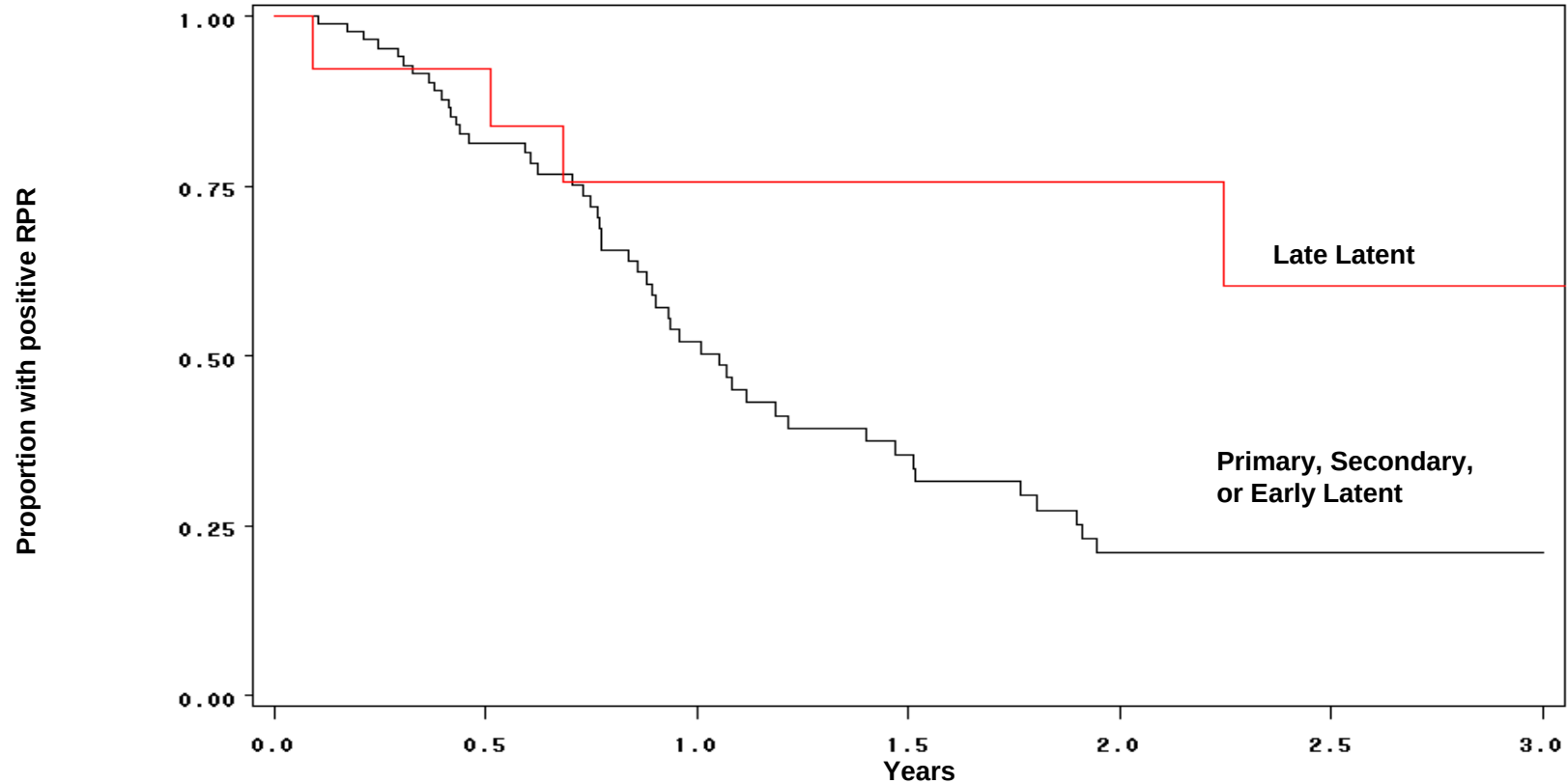


96% of patients had a 4-fold drop in RPR by one year.

Time to Negative RPR After Initial Treatment by Regimen



Time to Negative RPR After Initial Treatment by Diagnosis Stage



Late latent syphilis was associated with a longer time to negative RPR, $P=.02$.

- The incidence of primary and secondary syphilis in the United States reached its lowest rate in the year 2000.
- The rate of syphilis has since increased, notably among men, from 3.0 cases per 100,000 population in 2001 to 5.7 cases per 100,000 population in 2006.
- The CDC estimates the proportion of cases in MSM was 4% in 2000, 62% in 2004 and 2006. Up to 60% are HIV-infected, urban MSM .
- In New York City, the first quarter of 2007 saw a doubling of the number of syphilis cases, almost

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- The CDC estimates the proportion of cases in MSM was 4% in 2000, 62% in 2004 and 2006. Up to 60% are HIV-infected, urban MSM .
- In New York City, the first quarter of 2007 saw a doubling of the number of syphilis cases, almost exclusively in men, at least half of whom were HIV-infected and in regular follow-up with healthcare professionals.
- Rather than being recognized at the time of symptomatic presentation, many cases of early syphilis are discovered later by routine serologic testing.
- The aims of this study were to describe the presentation of syphilis in HIV-infected MSM, time to diagnosis and treatment, RPR response, and re-infection rates.

Baseline Information

- 18 patients were included:
 - Median age of 38 (IQ range 34-43),
 - Median CD4 of 399 cells/ μ L (IQ range 267-509)
 - 66 (56%) with HIV RNA <400 copies/mL.
- Median of 260 days (IQ 135-390) from the prior negative syphilis serology to the diagnostic test.
- 54 (46%) had a delay in diagnosis.