

Differences in presentation and outcome of subsequent episodes of syphilis in people living with HIV

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Leticia Espinosa[1], Juan Jorge Peris[1], Ana Moreno[2], Isidro Hernández[1], Ana Abad[2], **José L. Casado[2]**

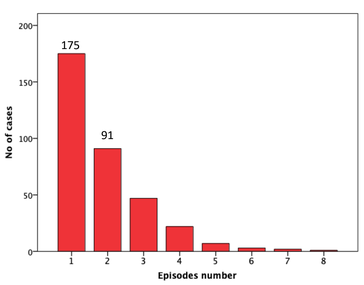
[1] Servicio de Medicina Interna. Hospital Universitario Sant Joan d'Alacant. Alicante. España; [2] Servicio de Enfermedades Infecciosas. Hospital Universitario Ramón y Cajal. Madrid. España

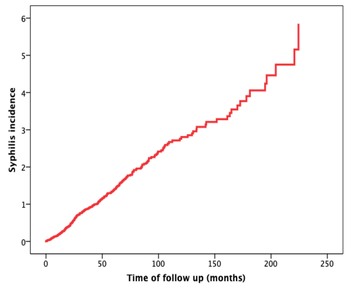
BACKGROUND

Identification of repeat episodes of syphilis in the same individual, particularly in people living with HIV (PLH), is increasingly frequent, and these individuals could present a less symptomatic disease. However, there are few data about the differences in serological presentation, rate of response, and persistence of serofast status according to subsequent episodes, an issue of clinical interest.

METHODS

Prospective cohort study of 348 episodes of syphilis observed in 175 PLH with regular follow up (508.3 person-years) in a HIV Unit in a tertiary hospital. Syphilis testing was routinely performed every 6-12 months in all the cases, and unscheduled visits were included in case of suspicion of syphilis or other sexually transmitted diseases. For this study, we explored a subgroup analysis restricted to individuals with a diagnosis of syphilis during the observation period and at least one subsequent syphilis test. We calculated syphilis incidence and repeat syphilis diagnosis per 100 person-years of follow-up from 2016 to 2024. The study was approved by the human research ethics committee of the Ramon y Cajal Hospital (248/16) and participants gave written informed consent.





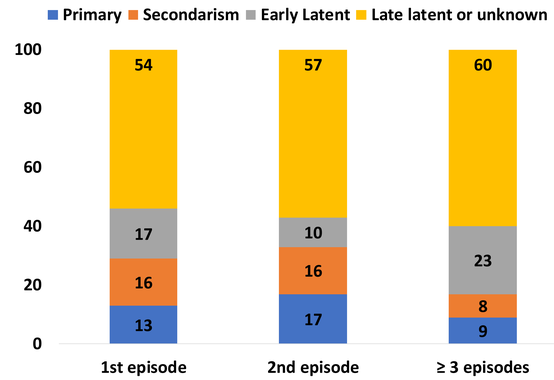
During median follow up of 35.4 months (IQR, 21.4-70.4), there were a total of 173 subsequent syphilis diagnoses following individuals' first-recorded syphilis diagnosis. The overall incidence rate was 54.3 cases per 100 person-years, after the 1st episode.

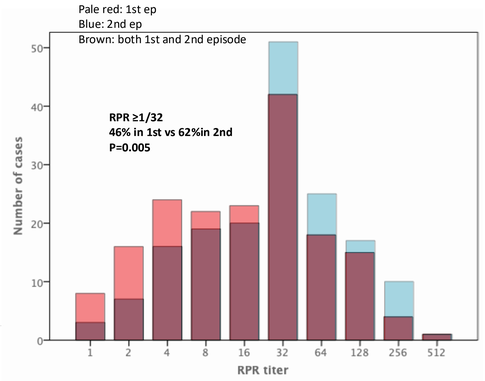
Syphilis diagnosis	1st episode N=175	2nd episode N= 91	≥ 3rd episode N= 82
Mean age (years, range)	48 (19-79)	48 (20-80)	50 (28-70)
Sex male at birth	174 (99)	91 (100)	82 (100)
Risk practice for HIV infection			
Former IVDU	3 (2)	1 (1)	-
MSM	165 (94)	89 (98)	82 (100)
Nadir CD4+ count (cells/mcL)	303 (193-420)	307 (181-422)	307 (167-421)
Nadir CD4/CD8 ratio	0.43 (0.24-0.6)	0.42 (0.23-0.58)	0.37(0.26-0.55)
Time of HIV infection (months,median)	101 (27-163)	89 (42-169)	73 (29-158)
cART at syphilis diagnosis	171 (98)	91 (100)	82 (100)
Time on current cART (months)	100 (27-163)	89 (42-169)	74 (29-158)
CD4+ count previous to 1st syphilis episode (cells/mcL)	686 (531-920)	716 (499-900)	721 (538-946)
Previous CD4/CD8 ratio	0.77 (0.9-1.02)	0.76 (0.52-1.12)	0.88 (0.58-1.17)

A previous episode of syphilis could change the clinical picture of successive episodes, but it does not decrease the incidence rate or serological presentation and does not alter the rate of response and RPR negativization of subsequent infections with *T. pallidum*.

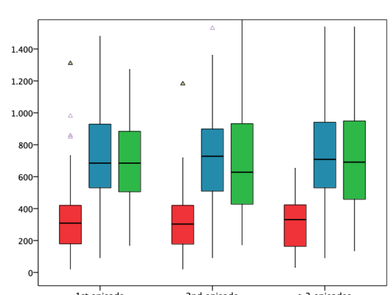
RESULTS

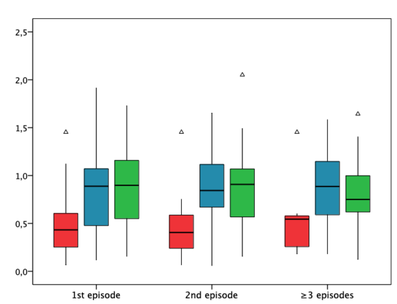
The form of presentation changes according to number of episodes (primary syphilis from 17 to 9%; secondary syphilis from 17% at the first, to 8% at those with a third episode). The presentation at the 2nd episode was similar, probably related to the close follow up. Also, serological presentation was similar according to successive episodes with even higher RPR titers in subsequent episodes.





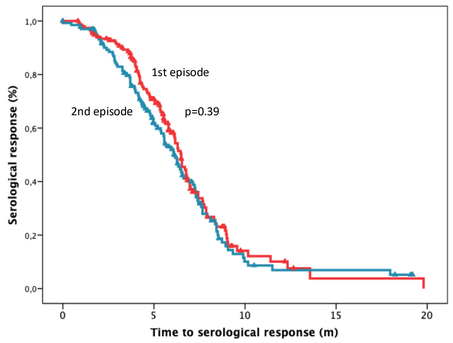
There were a decrease in the CD4+ count (-9.5 vs -11.9 cells/µ in 1st and 2nd), and in CD4/CD8 ratio (-0.03 vs +0.03), during the syphilis episodes, but this fall was similar and non statistically significant among the different episodes.

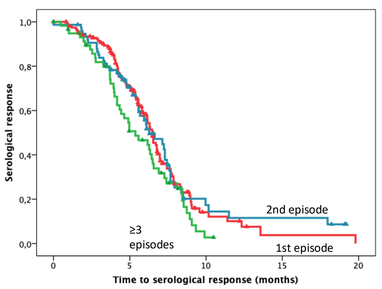


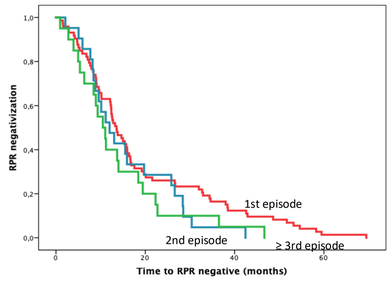


CD4+ count and CD4/CD8 ratio nadir (red), previous to the different syphilis episodes (blue) and at the syphilis diagnosis (green)

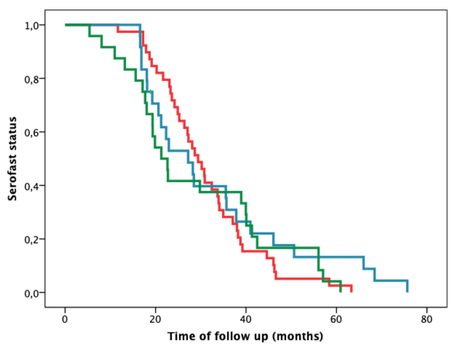
Despite a trend to a progressive shorter time, median time to serological response (5.5 vs 5.2 vs 4.8 months), or median time to negativization of RPR titer (13.6 vs 12 vs 10.8 months) was similar according to the 1st, 2nd, or ≥ 3 episodes.







Of note, the rate of serofast status was similar or higher in subsequent episodes (29% vs 32% vs 32%) whereas the time of persistence in the serofast status was similar.



CONCLUSIONS

As previously described, we observed that a previous episode of syphilis could (slightly) change the clinical picture of successive episodes (less primary or secondary syphilis), but, importantly, there was not a decrease in the incidence rate or serological presentation, neither a longer time to serological response, or time to RPR negativization of subsequent infections with *T. pallidum*.

Author Contact Information
Email: jcasado.hrc@gmail.com

Hospital Universitario Ramón y Cajal
Comunidad de Madrid