

A Retrospective Review of Neurosyphilis Cases at the Owen Clinic, University of California, San Diego

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Abstract

We report a retrospective analysis of 97 cases of neurosyphilis diagnosed at the Owen Clinic from 2003 to 2012. Diagnosis was based on symptoms, serum RPR titer, CSF WBC count, and/or CSF VDRL. There were 41 asymptomatic cases. Most cases had a serum RPR titer $\geq 1:32$ (87/97 cases), the cutoff for when to perform an LP. Most cases had a CD4 ≥ 200 (70/97), of which 53 cases were on HAART. Symptoms and/or CSF pleocytosis often factored into the management decisions. Of note, 42/97 cases had a CSF WBC < 10 whereas prior studies demonstrated a CSF WBC $>$ considered an indication for neurosyphilis treatment. Overall, treatment was consistent with the majority of cases a course of intravenous penicillin. With any guidelines, there will be missed cases. A high degree of suspicion based on symptoms and risk factors helped to account for the 10/97 cases with lower RPR titers.

Introduction

- The rate of neurosyphilis is high in HIV seropositive patients (1). This may be secondary to their underlying immunodeficiency.
- Patients with lower CD4 counts are at increased risk for developing neurosyphilis (2).
- Current CDC guidelines recommend a lumbar puncture in HIV-infected patients with CD4 counts <350 and RPR titers $>1:32$ with or without symptoms to rule out neurosyphilis (3).
- As this is a highly treatable infection, it is imperative to test and treat those with risk factors to prevent the potentially irreversible effects of neurosyphilis.

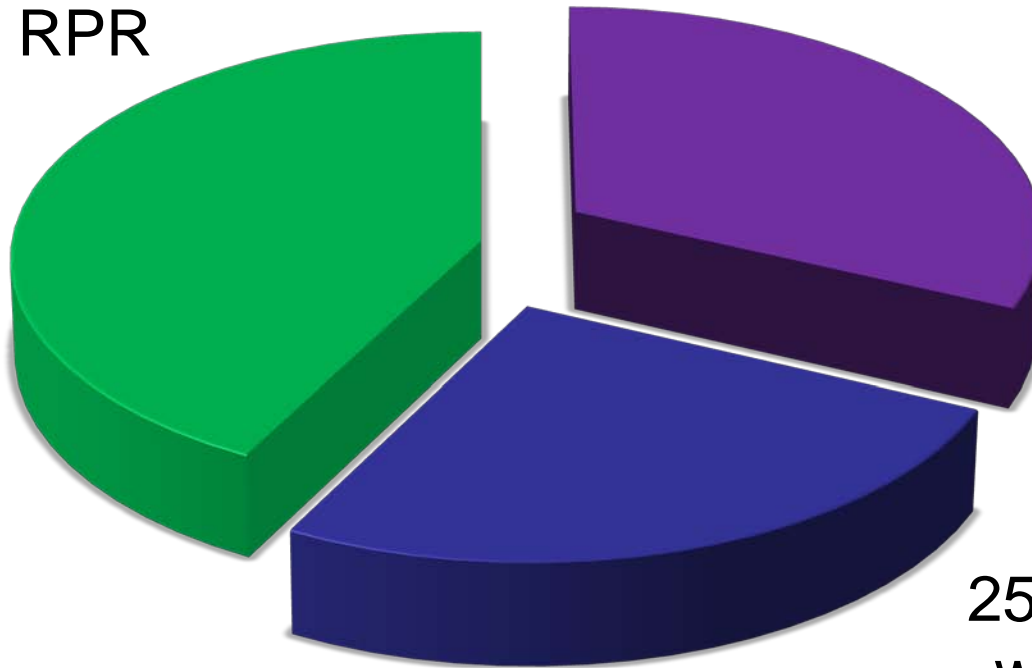
Methods

- Owen Clinic Database search for patients with ICD-9 Code 094.0-.9 for Neurosyphilis
- Medical Record Review of these patients narrowed to those who had lumbar puncture results
- 97 cases (8 cases of re-infection) were identified from 2003 to January 2013 with lab results and symptoms documented

41 patients had a prior positive RPR

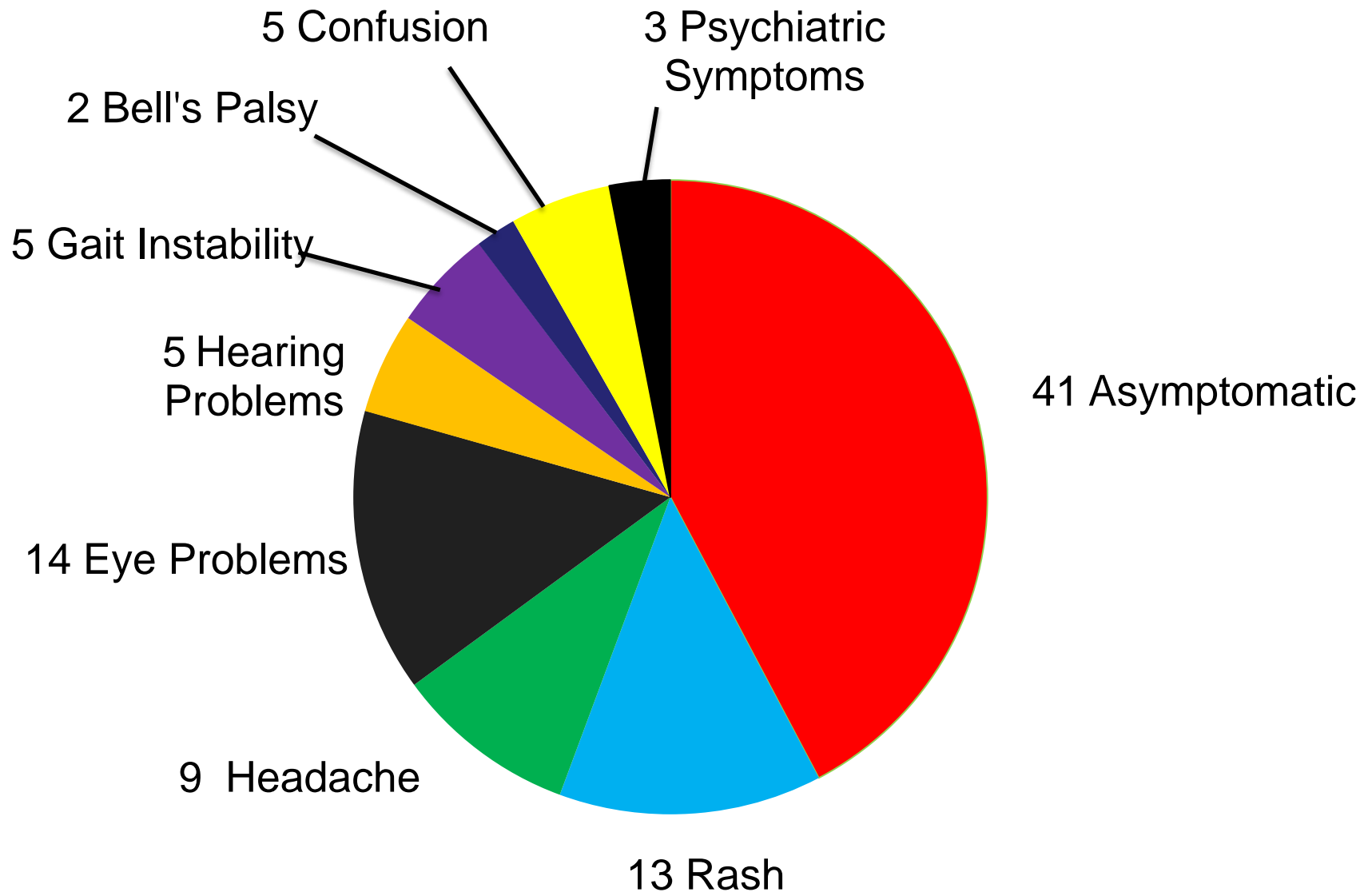
41 Patients
with Prior
Positive
RPR

31 Patients
with No
Prior RPR



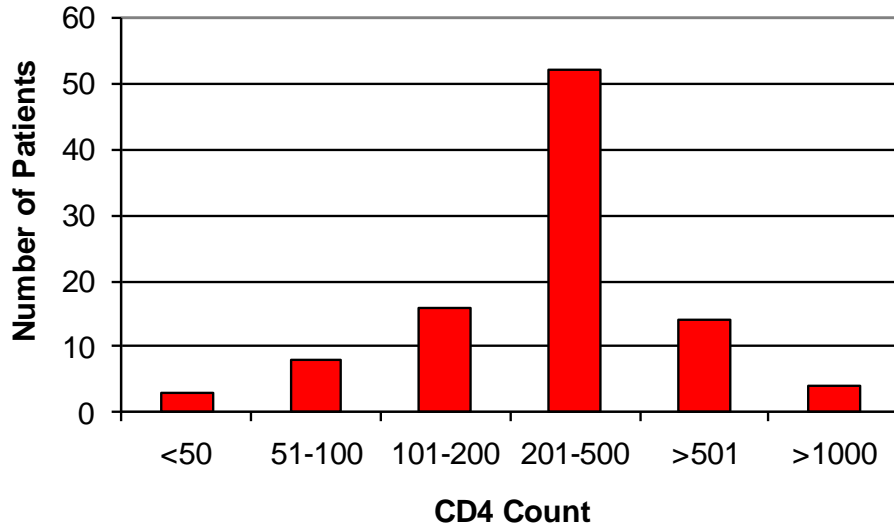
25 Patients
with Prior
Negative
RPR

Most patients were asymptomatic at time of neurosyphilis diagnosis



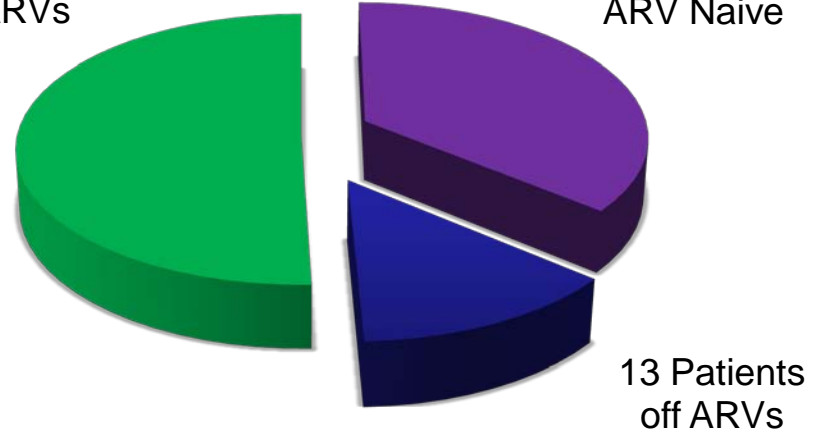
Most patients had CD4 counts >200

CD4 counts at time of Neurosyphilis Diagnosis

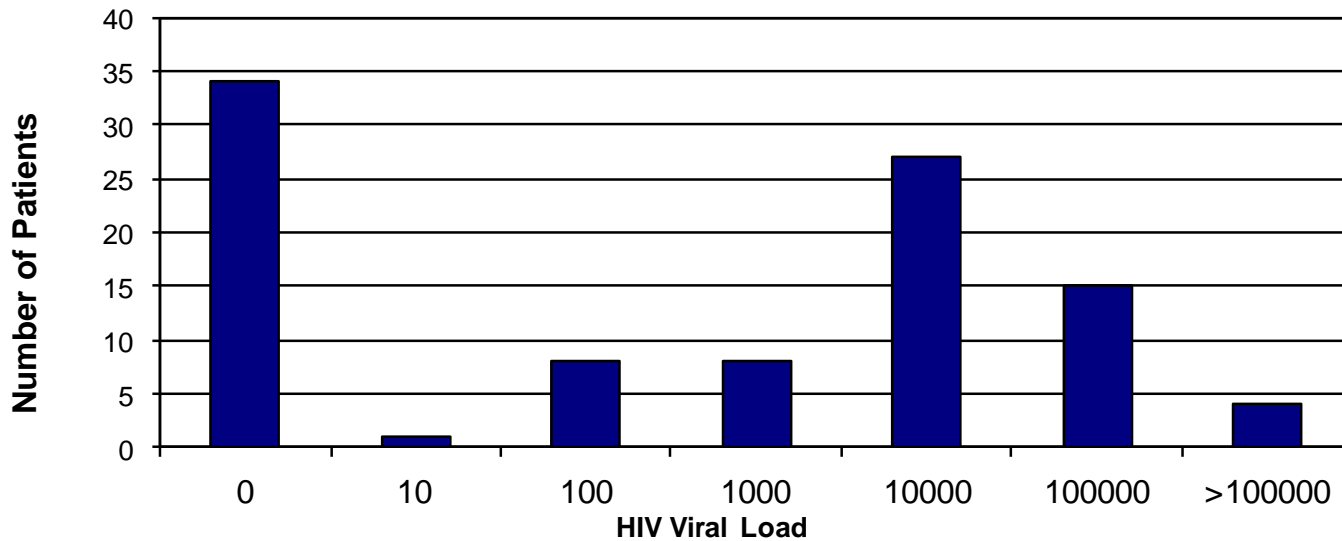


49 Patients
ARVs

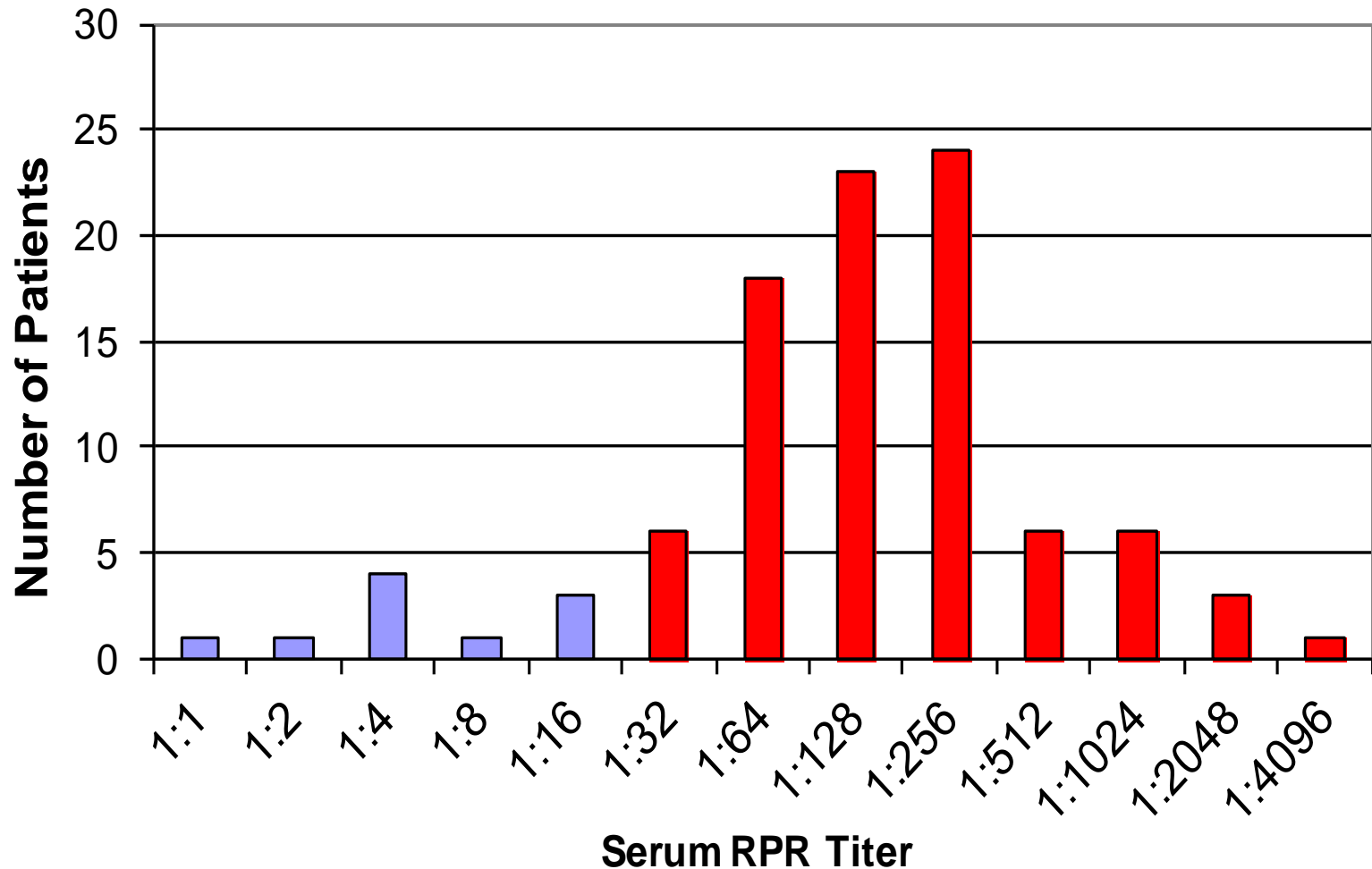
35 Patients
ARV Naive



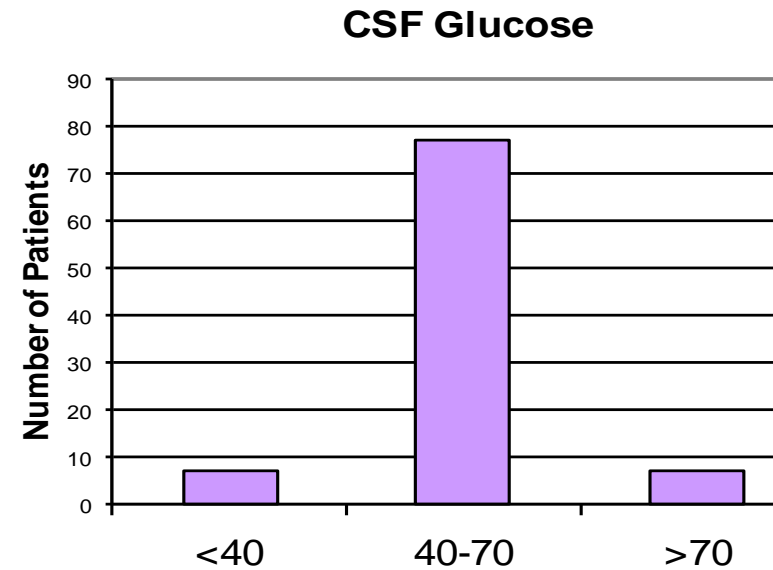
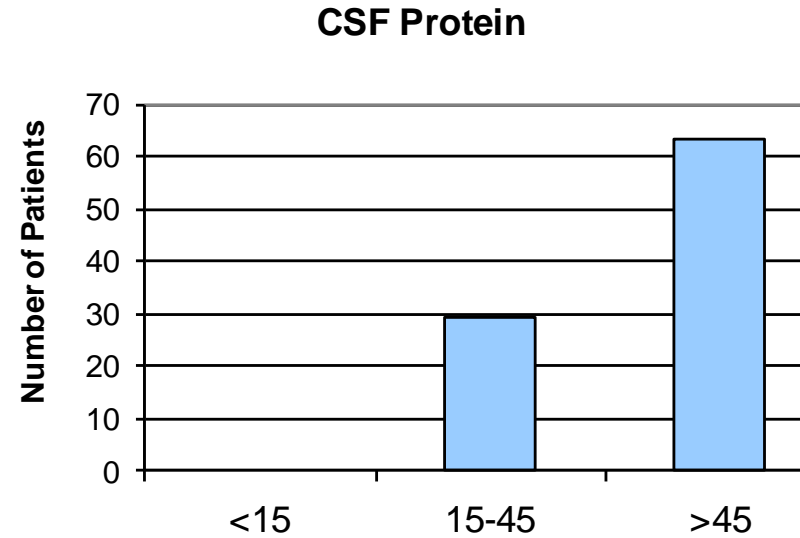
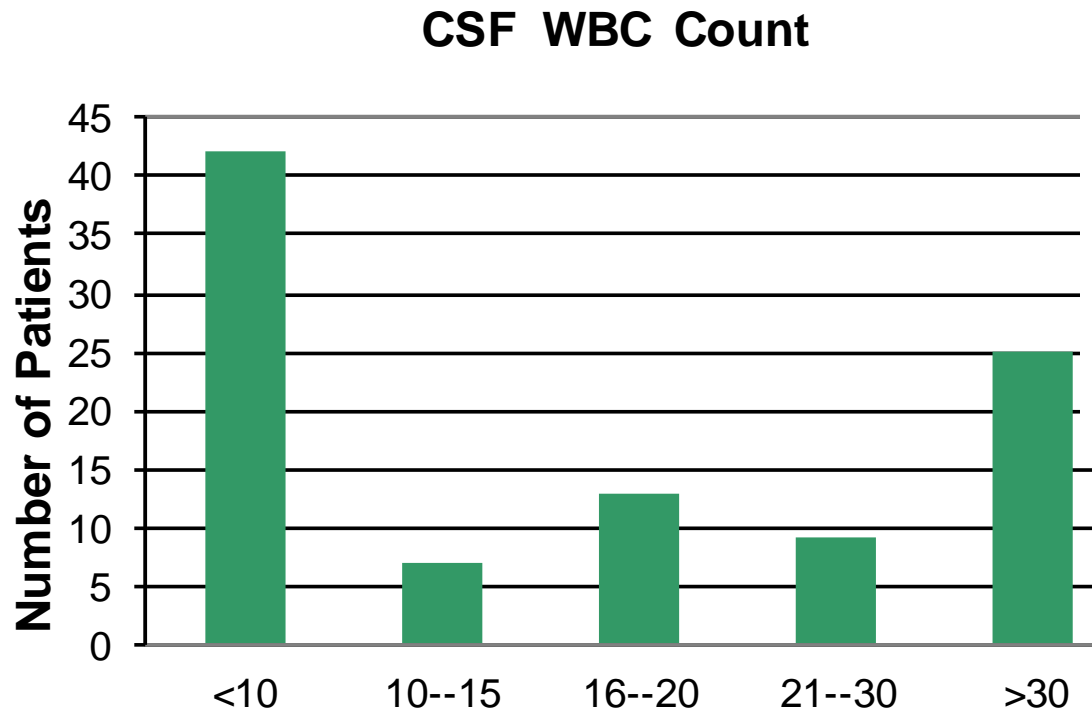
HIV Viral Load at time of Neurosyphilis Diagnosis



10 Patients had serum RPR titers <1:32 (Recommended threshold for lumbar puncture > 1:32)



42 patients had a CSF WBC <10



There were 31 patients with a Negative CSF VDRL

CSF VDRL	Number of Patients (Total=97)
Negative	31
Not Done	2
Positive	7
1:1	22
1:2	19
1:4	13
1:8	2
1:16	1

Clinical Characteristics in Patients with Negative CSF VDRL

Patients	CSF WBC	Symptoms	Serum RPR	Symptom Resolution
1	20	Headache	1:128	Resolved
2	21	Headache	1:2	Resolved
3	57	Rash	1:64	Resolved
4	41	None	1:64	
5	9	Headache	1:64	Resolved
6	37	Uveitis	1:256	Visual Defect
7	20	Gait	1:64	Unclear
8	1	Uveitis	1:1	Resolved
9	4	Otosyphilis	1:32	Hearing Loss
10	17	None	1:128	
11	38	None	1:128	
12	20	Gait	1:4	Unclear
13	12	None	1:1024	
14	9	Otosyphilis	1:256	Resolved
15	7	Otosyphilis	1:2048	Resolved
16	6	Pregnant	1:256	

Patients	CSF WBC	Symptoms	Serum RPR	Symptom Resolution
17	17	None	1:16	
18	18	Rash	1:128	Resolved
19	18	None	1:64	
20	2	Uveitis	1:64	Resolved
21	14	Bell's Palsy	1:16	Resolved
22	3	Dizziness	1:256	Resolved
23	9	None	1:4	
24	x	None	1:128	
25	30	Otosyphilis	1:64	Hearing Loss
26	9	None	1:32	
27	46	Uveitis	1:4	Resolved
28	73	None	1:64	
29	30	Headache	1:64	Resolved
30	17	None	1:256	
31	1	Bell's Palsy	1:64	Resolved

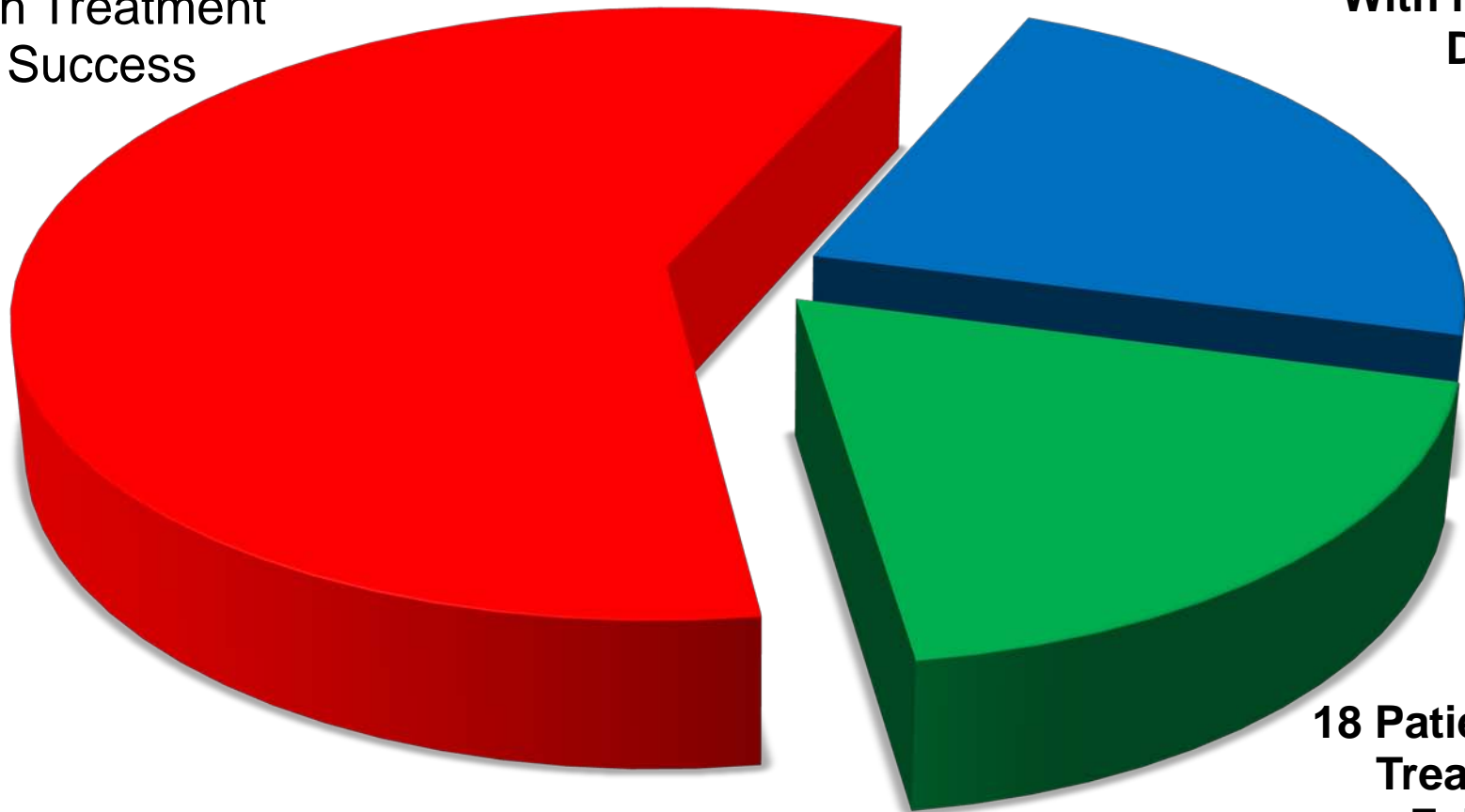
Characteristics of Patients for whom a CSF VDRL was not performed

1	16	Uveitis	1:128	Resolved
2	38	Rash	1:256	Resolved

Treatment success, defined as a 4-fold
Decrease in RPR by 6 months, was
observed in 57 patients

57 Patients
with Treatment
Success

22 Patients
With No Trend
Data



18 Patients with
Treatment
Failure

95 of 97 patients were treated with IV penicillin

- Of the 95 patients who received IV penicillin, 15 received additional intramuscular penicillin doses; 11 of these 15 were treated as an outpatient with intramuscular benzathine penicillin while awaiting LP results.
- 2/97 patients received benzathine penicillin alone.
 - Patient 1: CD4 255, VL 120K, HAART Naïve. RPR Titer 1:64 with rash. CSF WBC 57, Glucose 60, Protein 23, and Negative VDRL. Received 3 doses of IM penicillin. At 18 month follow-up visit, repeat serum RPR titer was 1:1.
 - Patient 2: CD4 308, VL 316K, HAART Naïve. RPR Titer 1:256. Asymptomatic. CSF WBC 20, Glucose 50, Protein 49, and VDRL 1:1. Received 2 doses of IM penicillin and did not follow-up.

Conclusions

- With increased screening, we find more cases of neurosyphilis
- A negative CSF VDRL is not 100% sensitive.
- There were 42 patients with evidence of neurosyphilis and a CSF WBC <10 .
- A combination of symptoms, serum RPR titer, CSF pleocytosis, and CSF VDRL are generally required to make appropriate treatment decisions in this setting.

References

1. Libois A, De Wit S, Poll B, et al. HIV and Syphilis: When to Perform a Lumbar Puncture. 2007. Sexually Transmitted Diseases. 34: 141-144.
2. Khalil GG, Moore RD, Rompalo AM, et al. Neurosyphilis in a clinical cohort of HIV-1 infected patients. 2008. AIDS. 22: 1145-1151.
3. Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep. 59: 1-110.
4. Marra C, Maxwell CL, Tantalo LC, Sahi SK, Lukehart SA. Normalization of Serum RPR Titer Predicts Normalization of CSF and Clinical Abnormalities after Treatment of Neurosyphilis, 2008. CID. 47: 893-899.
5. Marra C. déjà vu All Over Again: When to Perform a Lumbar Puncture in HIV-Infected Patients with Syphilis, 2007. Sexually Transmitted Diseases. 34: 145-146.

- UCSD IRB Approval #071931, Renewed 7/26/2012, Expires 7/26/2014.
- Owen Clinic Master Protocol: Retrospective Use of Existing Clinic Data.
- Supported by UCSD CFAR Core Services