

Lumbar Puncture In Late Latent Syphilis

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A. Rationale and Goals

The diagnosis and treatment of latent syphilis is a problem of renewed concern, since the incidence of syphilis has increased since 1986 and reports of treatment failure and rapid progression to neurosyphilis have accumulated in the HIV-infected population.¹ In the non-HIV-infected population, the rate of progression from asymptomatic neurosyphilis to the 2 symptomatic stage after treatment with intramuscular penicillin is 2% in 5 years. Because of this small number, the necessity of performing lumbar puncture in all patients with late latent syphilis has frequently come into question. Several studies have suggested that the regimens of intramuscular benzathine penicillin used for early syphilis are inadequate when given in the late latent stage for preventing progression to symptomatic neurosyphilis.^{3,4,5} The Centers for Disease Control had recommended that "ideally" all patients with latent syphilis for >1 year or of unknown duration undergo LP in order to identify those with asymptomatic neurosyphilis. In 1993, however, the CDC revised their recommendations to include LP only for patients with symptoms of tertiary syphilis and for patients at increased risk of developing symptomatic neurosyphilis.⁶ Evidence to support this change in recommendations has been deficient in several regards: most studies have had a small number of subjects, have had inadequate follow-up, and have not used optimal methods of study design because of valid ethical and practical concerns.

The purpose of our study is to determine

1. The prevalence of symptomatic and asymptomatic neurosyphilis in our study population
2. The frequency with which lumbar puncture is used in our study population
3. The factors which predict whether or not LP is performed on the study subjects
4. The frequency with which intramuscular versus intravenous penicillin is used in our study population
5. The change in serum RPR in response to treatment
6. The rate of development of symptomatic neurosyphilis in our study population and to compare the rates in subjects who have received lumbar puncture and appropriate treatment with those who did not undergo lumbar puncture.

B. Study Design and Statistical Analysis

a. Study design

Cross-sectional observational study.

b. Subject selection

See section G.

c. Crossover

None.

d. Randomization

None.

e. Duration of the entire study

1 year.

f. Repeated measurements

None.

g. Statistical analysis

Statistical analyses will include descriptive characteristics of the study population and bivariate analysis; SPSS/Windows will be used. Categorical data will be contrasted using the Mantel-Haenszel Chi square; when the expected value of a cell is less than 5, Fisher's exact two-tailed test will be used. To

compare continuous data, the Student's Nest will be used for normally-distributed variables (otherwise the Wilcoxon two-sample test). Multivariate logistic regression analysis will be conducted to explore the predictors of lumbar puncture.

C. Description of Study Procedures

No diagnostic or therapeutic procedures are involved in this study.

D. Study drugs

None.

E. Medical devices

None.

F. Study Questionnaires

Consent will be obtained through contact with the subjects' primary physician to mail questionnaires to the subjects including questions about specific neurologic symptoms but not containing any information about any subject's medical record.

G. Study Subjects and Methods of Recruitment

a. Eligibility criteria

The study subjects will include a randomly selected group of XXX patients in the Clinical Information System (CIS) who between 1989 and 1992 had positive serum RPR and FTA-Abs. The subjects will be men and women between the ages of 25 and 60. This study population will include those patients with CSF results that are either positive or negative for VDRL, and those with no CSF results entered. Patients with negative or unknown HIV status will be included.

b. Exclusion criteria

Patients with clinical evidence of primary, secondary, or early latent syphilis at the time of lumbar puncture, based on information obtained from their medical records, will be excluded. Patients with symptoms of tertiary syphilis, including neurosyphilis, at the index date (date of first positive RPR) will also be excluded. Patients who are known to have HIV infection are excluded.

c. Subject identification

Subject selection will be accomplished by a computerized search of our laboratory data base during the years 1989-1992 using the Clinical Information System at the Columbia-Presbyterian Medical Center (CPMC). Dr. PablosMdndez is a member of the staff.

d. Subject contact

Where applicable, consent will be obtained from the subjects through their primary physicians to mail questionnaires to the subjects as outlined above and to contact the subjects by phone. The telephone interview will consist of inquiries about neurologic symptoms and treatment with antibiotics.

e. Subject recruitment

Not applicable.

f. Gender or race restrictions

None.

H. Confidentiality of Data

No names, hospital medical record numbers or other identifying information will be kept in the data set, tubes with blood samples or the data study forms. Identifying information keyed to the study numbers will be kept by the Principal Investigator in a separate locked file. No subject will be individually identified by name or in any other way in any reports of this research.

I. Location of the Study

The study will be conducted in the office of the principal investigator in the Division of General Medicine.

J. Risks and benefits

There are no risks or benefits to study subjects. Benefits to society will include increased knowledge of the diagnosis and treatment of neurosyphilis.

K. Alternative Therapies

Not applicable.

L. Compensation and Costs to Subjects

None.

M. Minors and Research Subjects

No minors.

N. Radlation or Radioactive Substances

None.

O. Ref erneces

- 1 - Centers for Disease Control. MMWR. 1988; 37; 486-9.
2. Katz and Berger. Arch. Neurol. 1989; 46: 895-98.
3. Hahn, R.D. et al. Arch. Dermatol. 1956; 74: 355-66.
4. Smith, C.A. et al. Bull. WHO. 1956; 15:1087-96.
5. Fiumara. Sex. Trans. Dis. 1979; 6: 243-6.
6. Wolters, E.C. et al. J. Neurol. Sci. 1988; 88: 229-39.
7. Centers for Disease Control. MMWR. 1993; 42: RR-1 4.

Management of Late Latent Syphilis

Data Collection Form

Subject medical record # _____ Attending _____
 Date of birth _____ Sex M F _____
 Race: White__ Black__ Hispanic__ other__ Insurance Medicaid__ Medicare__ Privt__
 FTA-Abs _____ Date _____
 Serum RPR titers _____ Date _____ Location _____

LP done? Y N

CSF VDRL positive__negative__unknown__not done__ Date _____
 WBC _____ glucose _____ protein _____ Location _____

CSF VDRL titers _____ WBC _____ protein _____ Date _____
 Location _____

Symptoms of primary syphilis? Y N
 Symptoms of secondary syphilis? Y N

Symptoms of late syphilis (other than neurological)?
 aortitis__ gumma__ bone ds.__
 saccular aneurysm__ skin lesions__ joint ds.__

Symptoms or signs of neurosyphilis?
 personality change__ hypoactive or absent reflexes__
 ataxia__ optic atrophy__
 stroke__ sensory changes__
 vision changes__ pupillary abnormalities__

hearing loss__
paresthesias__
bladder dysfunction__
bowel dysfunction__
seizures__
headache__

cranial nerve palsies__
dementia__
psychiatric disturbance__
Romberg's sign__
Charcot's joint__
hypotonia__

Treatment: 1 BPG__ I.V. pen G__
2 BPG__ other_____
3 BPG__ Date_____ Location_____

HIV test positive negative unknown not done Date_____

HIV risk factors 0__ 1__ 2-3__ >3__

CD4 count _____ Date_____

Clinical AIDS? Y N

Attending characteristics:

Age__ Sex M F

Year of graduation/ M.D. awarded_____

Primary Care__ Infectious Disease__ Other Int. Med. subspecialty__
Neurologist__ Specialty other than I.M. or Neuro__

Infectious Disease consult? Y N

LP recommended? Y N