Cerebrospinal Fluid Serology—Is its Routine Use Justifiable?

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DESPITE A RESURGENCE OF INFECTIOUS SYPHILIS in the United States during the past 15 years, the incidence of late complications has been declining. Only 14 cases per 100,000 population were reported in the United States during fiscal year 1975 (*1*)—an all-time low. One case of tertiary syphilis was reported in Colorado in 1975. However, as shown in the table, requests for cerebrospinal fluid (CSF) serologies (both Venereal Disease Research Laboratory (VDRL) slide and fluorescent treponemal antibody absorption (FTA-ABS) tests) have been increasing in that State. Because of the low yield, we surveyed physicians to determine their criteria for requesting CSF-VDRL tests. We did not include CSF-FTA-ABS requests in the survey because performance of this test was suspended in late 1974.

Results of CSF-VDRL and CSF-FTA-ABS tests in Colorado, 1969–75

Year	CSF-VDRL			CSF-FTA-ABS		
	Total performed	Reactive		Total performed	Reactive	
		Number	Percent		Number	Percent
1969	363	6	1.7	.....	.....	.....
1970	355	5	1.4	.....	.....	.....
1971	689	3	0.4	.....	.....	.....
1972	720	8	1.1	17	5	29.4
1973	780	2	0.3	47	[1]14	29.8
1974	729	4	0.5	74	23	31.1
1975	1,106	6	0.5	.....	.....	.....

[1] Borderline.

Study Method

We mailed questionnaires to all physicians who had requested CSF-VDRL tests from the Colorado Department of Health Serology Laboratory from March to September 1975. This laboratory performs the majority of blood VDRLs ordered by private practitioners in the State and by physicians of the University of Colorado Medical Center (UCMC); it performs almost all the CSF-VDRLs in the State. We asked each patient's age, sex, race, and diagnosis; the reason for ordering the test; the final diagnosis; and the physician's date of graduation and specialty.

Results

Questionnaires were returned by 81 physicians in community hospitals for 173 patients, by 49 UCMC physicians for 114 patients, by 33 physicians in private practice for 41 patients, and by 8 physicians at Kaiser Permanente for 9 patients. However, one-third of the questionnaires were not completely filled out. In reporting the results, we cite the number of completed responses.

There were 163 males and 174 females; their ages ranged from 3 weeks to 88 years, with a median of 44 years. In 9.8 percent of the patients, neurosyphilis was suspected based on clinical evidence and in another 27 percent, the tests were requested in order to rule out neurosyphilis. Neurosyphilis was suspected in 2 or 1.4 percent of 145 patients under age 40 and in 31 or 23.5 percent of 132 patients over age 40.

The CSF-VDRL laboratory form requests information on concomitant blood VDRL studies. A review of these forms and all other files on blood VDRL tests at the health department laboratory revealed no available results for 63 percent of the 337 study patients. Of the 137 blood serology reports available for study patients, only 18 indicated reactivity. Among the 33 patients suspected of having neurosyphilis, 14 had reactive blood serologic tests, 6 had nonreactive serologic tests, and 13 had no record of a recent blood serology.

Of the 33 patients suspected of having neurosyphilis, only an 88 year-old man with symptomatic neurosyphilis had a positive CSF-VDRL. The only other positive test occurred on a specimen obtained during a myelogram on a patient not suspected of having syphilis. She was later lost to followup, and her physician could not provide clinical details or reports of blood serologic tests to determine if syphilis should have been suspected.

The responding physicians indicated alternative diagnoses for 85 percent of the patients in whom neurosyphilis was not suspected; 62 percent of these diagnoses were classified as neurological or psychiatric and 20 percent as neurosurgical or orthopedic. Two-thirds of the respondents reported having a specialty; among these, neurologists, neurosurgeons, and orthopedists accounted for one-half of the physicians who performed lumbar punctures. Of the respondents whose specialty was indicated, approxi-

mately one-half had graduated from medical school between 10 and 20 years earlier.

Comment

Meningeal invasion by *Treponema pallidum,* usually considered a late event, occurs in one-third to one-half of the patients who have early infectious syphilis; however, symptomatic syphilitic meningitis is rare (*2*). Neurosyphilis (tabes dorsalis, paresis, meningovascular syphilis, or a combination of these) occurs in approximately 10 percent of untreated patients 5 to 35 years after the onset of infection (*3*). Diagnosis has become increasingly difficult as the incidence of neurosyphilis has diminished and its modes of presentation have changed (*4, 5*).

Estimates of the predictive value of specific laboratory tests vary according to the criteria used by the investigator for assigning a diagnosis of neurosyphilis. Recently introduced tests have been especially difficult to evaluate because of the decreased prevalence of the disease. The reactivity of blood serologic tests appears to be 70 percent for the VDRL and 95 percent for the FTA-ABS (*3*). Although a lumbar puncture is recommended to differentiate late latent syphilis from asymptomatic neurosyphilis in patients with reactive blood serologic tests, adherence to this dictum seems to be uncommon. A careful neurological and psychiatric examination to rule out symptomatic neurosyphilis followed by treatment for asymptomatic neurosyphilis is current accepted clinical practice in lieu of a lumbar puncture (*6*).

Neurological or psychiatric abnormalities combined with abnormal blood serology are clear indications for the performance of a lumbar puncture, which remains the definitive diagnostic procedure. Elevated CSF white-cell count and protein are the most sensitive indicators of disease activity. A reactive CSF serology is diagnostic, but reports of CSF-VDRL reactivity range from 60 to 98 percent. Although CSF-VDRL specificity is high, false-positive results may occur when CSF is contaminated during traumatic lumbar puncture. As little as 0.050 ml of blood from a patient with a VDRL titer of 1:1 added to 1 ml of CSF can cause VDRL reactivity (*7*). However, to cause a false-positive result, even with a blood serology titer of 1:256, the CSF specimen tested must be visibly bloody.

CSF-FTA and FTA-ABS tests have been recommended as sensitive indicators of neurosyphilis (*8*). The large percentage of reactive CSF specimens when the test was performed in Colorado suggests that problems may occur in the field. Difficulties have been encountered in the performance of the blood FTA-ABS test (*9*). Because insufficient numbers of spinal fluids from nonsyphilitic patients have been tested and because of the occurrence of positive CSF-FTA-ABS tests in patients without any evidence of syphilis, in 1975 the Center for Disease Control recommended that FTA tests not be done on spinal fluid until further studies of their specificity were completed (*10*). In one such study, 1 of 177 nonsyphilitic patients had a reactive FTA-ABS test, but 5 of 15 syphilitic patients with no other evidence of neurosyphilis had reactive tests. The authors concluded that "without other supporting clinical or laboratory data, the diagnostic value of a reactive CSF-FTA test is unknown" (*11*).

From our survey findings, it is clear that most CSF-VDRLs are being ordered routinely rather than selectively. The test is being ordered for young patients without evidence of syphilis by physicians who perform lumbar punctures as a consequence of their clinical specialty. A diagnosis of syphilis was considered in only 9.8 percent of the 337 patients. Neurosyphilis was definitely diagnosed in only one patient. Furthermore, the results of the blood serology were unavailable for 63 percent of the study patients and for 13 of the 33 patients in whom neurosyphilis was suspected.

The CSF-VDRL is apparently being used to detect cases of an extremely rare disease in a population with low prevalence. Physicians may well be adhering to teachings of 30 years ago when the prevalence of neurosyphilis was higher. It appears that the routine performance of a VDRL on all CSF specimens is still being recommended to house staff. This con-

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clusion is suggested by the finding that one-third of the requests came from physicians at the university hospital. A natural tendency to perform tests just because they are available may also be a factor (*12, 13*), especially since CSF specimens are not easily obtained and one may want to get the "most" out of the specimen. As with other tests ordered routinely, even when test results are abnormal they may be ignored (*12, 13*).

Although our survey was specifically concerned with CSF serology, we believe that the following general conclusions can be drawn from the results: (*a*) tests that are appropriate for diagnosis provide little or no useful information when used for case detection in a low-prevalence population, and in fact they can be misleading (*9*); (*b*) the usefulness of such tests depends on appropriate preliminary testing and prompt review of all results by the physician; and (*c*) habit plays an uncomfortably large role in medicine. Standard medical practice should be continually reconsidered in light of the changing epidemiology and biology of diseases. This principle must be taught to students, since today's common disease may be tomorrow's rarity.

Recognizing that spontaneous change of behavior by individual physicians is difficult to achieve, we suggest that directors of laboratories performing CSF-VDRLs are in a unique position to educate and effect change. The CSF specimen sent in for serologic testing can be held, and the director can communicate personally with the physician. Alternatively, the test request can initiate a query concerning the indication for the test, blood serology data, and pertinent clinical information. In view of the growing evidence of unnecessary laboratory testing (*12, 13*) and the need to control health care expenditures, such educational exchanges should become common practice in public health and university hospital laboratories.

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SYNOPSIS

DANS, PETER E. (University of Colorado Medical Center, Denver), VERNON, THOMAS, and RUSSELL, BARBARA: *Cerebrospinal fluid serology—is its routine use justifiable?: Public Health Reports, Vol. 92, May–June 1977, pp. 260–262.*

Although neurospyhilis has become a rare disease, requests for cerebrospinal fluid (CSF) syphilis serology tests at the Colorado Department of Health have increased in recent years. Because of the low rate of positive results, questionnaires were sent to the physicians who requested these tests to determine the criteria for their use. Neurosyphilis was neither suspected nor an important consideration to rule out in 63 percent of the 337 patients sampled. Of the patients whose ages were specified, more than half were under age 40. No concomitant reports of blood serology were available for 63 percent of the study patients, and only 13 percent of the available blood serology reports indicated reactivity. One of the two patients with positive test results was appropriately treated, but the other patient for whom the test was ordered "routinely" to rule out neurosyphilis was lost to followup. One-half of the tests were requested by neurologists, neurosurgeons, and orthopedists.

The survey findings indicated that most of the CSF serologic tests for syphilis were done without appropriate preliminary testing for patients who had no evidence of syphilis by physicians who perform lumbar punctures as a consequence of their specialties. The authors recommend that use of the test be reviewed in light of the changing epidemiology of the disease. They further suggest that directors of laboratories performing CSF serologic tests are in a unique position to initiate an educational exchange and a consequent change in physicians' behavior.