USEFULNESS OF ROUTINE SEROLOGIC TESTS FOR SYPHILIS

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ROUTINE serologic tests for the detection of syphilis recently have received criticism relative to their usefulness and cost. The most severe criticism has been leveled against the obligatory premarital blood test that is said to detect relatively few cases of previously undiagnosed syphilis and at a comparatively high cost per test.[1] This concept of the worth of these routine serologic procedures is a reversal of the earlier opinion that the procedures are essential to our national welfare. The earlier opinion resulted in the passage of laws in 40 of the 48 states invoking compulsory premarital examination, and also has affected the standards established by accreditation boards for hospitals.[2] On the other hand, routine serologic tests for syphilis continue to have staunch supporters, especially among public health workers.[3-5] Collen and Linden[6] reported favorably on the usefulness of serologic screening in prepaid group-practice plans.

Magnuson, Donohue, Stuart, and Gleeson[7] of the Public Health Service recently discussed the advantages of premarital serologic tests for syphilis, which in most states are part of a physical examination. Among the advantages listed are: detection of syphilis; prevention of transmission of syphilis between marital partners; provision of the physician with an opportunity to give health education, sex education, and marriage counseling; detection of other diseases; and provision of an index of the prevalence of syphilis. These authors stated that reactivity rates in premarital blood testing had not declined in the years 1951-1954, the only period for which data were available, and that conservative estimates indicated that 12,000 to 13,000 persons having previously untreated syphilis were found annually through premarital blood testing. They expressed the belief that if through the premarital blood testing only a small percentage of these persons were protected from infecting their subsequent spouses and thereby avoiding congenital syphilis in their offspring, routine testing would result in the prevention of a considerable number of new cases of syphilis.

Since the opening of the Cleveland Clinic in 1921, serologic tests for syphilis have been performed as one phase of our routine laboratory survey, which consists of determination of hemoglobin concentration, cell volume, white blood cell count, blood sugar value, and urinalysis. This work is part of the routine examination of all new patients and any former patients for whom complete re-examination is requested.

Because it has been our belief that the routine serologic tests are useful, it was decided to review our records to determine more accurately the status of

these tests. Since we routinely perform both the Kolmer complement-fixation test and the Kahn test, the records also were analyzed to ascertain the relative merits of the two tests.

Material and Method

Data were analyzed on the basis of three groups of findings: group I comprised findings in 340 patients in whom serologic tests for syphilis were positive; group II comprised findings on 501 premarital serologic tests; group III comprised findings on serologic tests of approximately 3,000 professional blood donors.

All of the specimens included in the study were examined by using both the Kolmer complement-fixation test and the Kahn test. The antigen used in the two-tube complement-fixation test was Kolmer's cardiolipin antigen prepared by the Sylvana Chemical Company. The three-tube Kahn test followed the usual accepted Kahn technic, using the Standard Kahn Antigen prepared in Doctor Kahn's laboratory at the University of Michigan. All tests in which the results were positive or doubtful were repeated and then the specimens were submitted both to the Kolmer and to the Kahn quantitative procedures.[8] When it was requested by the attending physician, sera were referred to the serology laboratory of Mount Sinai Hospital, in Cleveland, for the Kline test, or to the University of Michigan for the *Treponema pallidum* immobilization (TPI) test.

Group I. This group includes those patients in whom serologic tests for syphilis were positive. Review of 12,396 blood specimens that were submitted to our laboratory for serologic tests for syphilis during a four-month period (June 1 through September 30, 1955) showed that 516 specimens from 340 patients were reported as positive.

Of the 12,396 specimens, 9,851 were from new patients who were undergoing routine laboratory surveys. Most of the others were from former patients who were being restudied; however, a small number of these specimens were submitted for premarital blood tests, for pre-employment surveys, or for rechecking a previously reported positive test.

A complete review was made of 313 charts, and it was possible to subdivide the group of patients as follows: 114 newly admitted patients having syphilis; 64 patients in whom syphilis had been previously diagnosed here; 60 patients having biologic false-positive tests for syphilis; and 75 patients for whom complete follow-up data were not available. The differentiation for the first two subgroups was an arbitrary one. Among those classified as newly admitted patients having syphilis were included all patients in whom the diagnosis of syphilis had not previously been made here, even when the diagnosis had been made elsewhere prior to the patient's being seen here.

The greater sensitivity of the complement-fixation test as compared with the Kahn test is obvious from the results in the 114 newly admitted patients. Sixty-

one, slightly more than half (Table 1), of the 114 diagnoses were based on the serologic findings and would not have been made if the routine serologic tests had not been performed. The results of the Kolmer test were positive in all but 2 of the 114, and in approximately one third of these patients there was a negative Kahn in the presence of a positive Kolmer test. Twenty-five of the 61 patients in the first two categories listed in Table 1 began treatment here, while most of the remainder were treated elsewhere. Of the entire group there was only one patient with primary syphilis who, at the time of admission, had positive findings on dark-field examination.

Table 1.—*Basis of diagnosis in newly admitted patients having syphilis, during a four-month period*

Basis of diagnosis	Results of serologic tests, no. of patients			Total no. of patients
	Kolmer *positive* Kahn *negative*	Kolmer *negative* Kahn *positive*	Kolmer *positive* Kahn *positive*	
Serologic test alone, no history of disease admitted	6*	2	21**	29
Serologic test, history of infection obtained subsequently	8	0	24**	32
History of infection given on admission, confirmed by serologic test	14	0	22	36
Clinical symptoms suggesting syphilis, confirmed by serologic test	8	0	9	17
Total	36	2	76	114

**TPI test performed on 2 specimens, result positive in each.*

***TPI test performed on 1 specimen, result positive.*

Many of the 64 patients having previously diagnosed syphilis had been coming to the Cleveland Clinic for years, and the initial diagnosis of syphilis had been made and treatment had been instituted here. An analysis of these data in treated syphilis (Table 2) continues to demonstrate the greater degree of sensitivity of the Kolmer test as compared with the Kahn test.

Table 2.—*Results of serologic tests in patients having previously diagnosed syphilis, during a four-month period*

Results of serologic tests	Number of patients		
	Symptomatic for syphilis at time of serologic tests	Asymptomatic for syphilis at time of serologic tests	Total
Kolmer *positive*) Kahn *positive*)	7	28	35
Kolmer *positive*) Kahn *negative*)	6	18	24
Kolmer *negative*) Kahn *positive*)	3	2	5
Total	16	48	64

Sixty patients were classified as having biologic false-positive tests because there was no evidence to suggest syphilitic infection except positive results of either the Kolmer or the Kahn test or both, or there was a clinical diagnosis in which a false-positive serologic test for syphilis was a common finding. Each attending physician had his own method of arriving at the decision to accept the result of our determination as being false-positive (Table 3). The clinical features that seemed to exclude syphilis are represented in a variety of cases. For example there was an 80-year-old moribund woman who previously had had numerous negative serologic tests here; and there was a five-year-old boy who before had had many negative serologic tests for syphilis and whose parents had negative serologic tests and no history that might indicate association with the disease. Repeated serologic tests were negative in 19 (almost one third) of the 60 patients. This percentage of repeated negative serologic tests compares favorably with the experience of other workers.[6]

In those patients regarded as having false-positive tests the high degree of sensitivity of the Kolmer test with its associated lack of specificity is shown to be a disadvantage, since nearly half of the false-positive tests reported were on the basis of positive Kolmer and negative Kahn tests.

The final subgroup consists of the 75 patients for whom complete follow-up reports were not available. Twenty-five of the 75 patients were treated here for another disease and were referred back to their own physicians for follow-up of their positive serologic findings. Another 15 of the 75 were too ill from other diseases to be concerned about positive serologic tests; most of these patients had malignant neoplasms and died during the course of the study. Three patients of the subgroup failed to return to the Clinic for further study.

Group II. During the six-year period of the survey (March 10, 1951, to March 10, 1957), 501 persons had the special premarital serologic tests which are

Table 3.—*Basis for classification of false-positive serologic tests during four-month period; all patients asymptomatic for syphilis*

Basis for classification	Results of serologic tests, no. of patients: Kolmer *positive* Kahn *negative*	Kolmer *negative* Kahn *positive*	Kolmer *positive* Kahn *positive*	Total no. of patients
Clinical situation excluded syphilis	9	2	12	23
Clinical situation excluded syphilis, but recheck serologic test recommended	2	0	1	3
Repeated serologic test *negative*	14	3	2	19
Kline test *negative*	0	0	2	2
Cerebrospinal fluid test *negative*	1	0	4	5
Cerebrospinal fluid test and TPI test *negative*	1	1	2	4
TPI test *negative*	1	1	2	4
Total	28	7	25	60

performed in conformity with the law of the State of Ohio. No new cases of syphilis were found. Seven patients whose serologic test results were reported as positive were under treatment at the time or had completed their treatment here or elsewhere.

A review of this roster of premarital applicants indicates that it was not a cross section of the general population but was heavily weighted by a large number of professional people and their families, who as a population group have an extremely low incidence of syphilis. Twenty-five (5 per cent) of the 501 persons listed on the roster were physicians.

Group III. During the past seven years (1950 to 1957), we have drawn 11,958 units of blood from approximately 3,000 professional donors. Of this group only three potential donors have been rejected because of positive serologic determinations for syphilis. In each case an interview indicated that the person although unaware of his infection was not surprised by the positive results. In all three patients treatment was instituted promptly. Group III is similar to the premarital group in that it also is not representative of the general population, as many of the donors are students in colleges or professional schools, or are

members of our staff or are our employees, groups that would be expected to have a low incidence of syphilis.

Discussion and Summary

Routine serologic tests for syphilis appear to be useful. Not only are many cases of previously undiagnosed syphilis found, but attention is focused on many previously diagnosed cases, some of which require more adequate treatment. Some patients are inaccurate in answering questions about a possible history of venereal disease, and sometimes even in the presence of unmistakable clinical evidence they will admit to having a history of syphilis only after a positive serologic test has been reported to them. The importance of accurate diagnosis is obvious. While many of the newly admitted patients having syphilis had had previous medical care, it is important that the diagnosis be recognized at the time of the routine test, for the sake of sound medical practice. However, a goodly number of these patients (32 of 114) classified as newly admitted patients having syphilis did receive treatment at the Cleveland Clinic either during the time covered by this survey or subsequently.

The performance of the sensitive Kolmer complement-fixation test appears to be excellent. In a test of this type, sensitivity is obtained at the expense of specificity; nearly half (28 of 60) of the false-positive serologic tests were based on positive Kolmer tests and negative Kahn tests. However, 60 of the 177 diagnoses of syphilis would have been missed on the initial survey if only the Kahn test had been used. The usefulness of the Kahn test is related to its specificity; only seven of the patients having false-positive tests had been reported to have a positive Kahn test and a negative Kolmer test.

The usefulness of the premarital blood test seems to be slight in our clinic practice. Although the series is too small to be really significant, nevertheless the results indicate that premarital serologic tests for syphilis have little application in the population served by us.

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