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SEROLOGIC INTERPRETATION IN THE DIAGNOSIS OF SYPHILIS

EDWIN H. CRESSMAN
Professor of Dermatology and Syphilology

"But I see an incredulous look upon some faces and I hear the whispered comment—'is heard often enough! 'Where is all this syphilis? It does not come my way.' Yes, it does. The syphilis we see but do not recognize, everywhere awaits diagnosis, so protean are its manifestations."

Sir William Osler.

A GREAT mass of the population moves among us infected with syphilis—men, women, and children, awaiting diagnosis. The number of syphilitics in this country has been conservatively estimated at 12,000,000. The recent draft of men for military service has shown that the incidence of syphilis (ages 21 to 35) among negroes is 27.2 per cent, and among whites 2.35 per cent, or among the entire male population in this age group, 4.77 per cent. Furthermore, in the above analysis of Vonderlehr and Usilton it was shown that the prevalence of syphilis in whites was almost doubling each 5 years of life, ages 21 to 25—1 per cent; ages 26 to 30—2 per cent; ages 31 to 35—3.77 per cent.

Within the past few years physicians have performed an ever increasing number of serologic examinations for syphilis. Premarital and prenatal laws, the routine test for hospital patients, food handlers, domestic servants, large industrial groups, military service, Red Cross blood donors, and many other routine tests have led to the discovery of many new cases. Skin eruptions, rickets, rheumatism, heart disease, and neurologic disorders which many times would go unrecognized are being found to be due to syphilis. We have come at last to the unmasking of the "great masquerader."

With all of this has come many problems, and by no means least of these problems is that of the interpretation of the serologic tests. Does this patient who has a positive reaction have syphilis, or is this a false reaction? Am I justified in starting this patient who has a positive serologic test and no symptoms upon a long and arduous course of antisyphilitic treatment which is both expensive and hazardous? Does this patient with the little stabbing pains and the negative blood have neurosyphilis? —et ad infinitum.

The serologic tests for syphilis attain a high degree of accuracy when the report comes from a good laboratory, but the fact remains that at times a positive result may be obtained in a patient who does not have syphilis, and the converse of this, a negative result, may be obtained in the patient who is infected. Many errors of diagnosis are the result of inaccurate information among the profession. Perhaps this may be more clearly understood by citing several cases as examples:
Case I. Mr. C. F., age 48, complained of ptosis of the right eyelid and a slight upward rotation of the right eyeball. The patient consulted an ophthalmologist. Examination of the eyes and recording of the blood pressure was the extent of the examination. No serologic test was performed. The patient was told to forget it, that it would soon return to normal, and that there was nothing serious wrong. Over a period of a few weeks the condition did gradually correct itself and was promptly forgotten. Two years later in preparation for a contemplated operation for a cataract which had been developing, a blood serologic test was found to be positive for syphilis. Examination at this time revealed exaggerated patellar reflexes, and the patient had noticed a slight toe slapping. The spinal fluid was negative, but the blood was repeatedly positive.

Diagnosis: Neurosyphilis—early tabes.

Comment: A serologic test for syphilis should have been performed by the ophthalmologist. Paralysis of the muscles of the eye is not an uncommon symptom of neurosyphilis. This neglect resulted in two years' delay during which destructive changes in the nervous system could have been great. Fortunately, in this case, the outcome was satisfactory. Under treatment the toe slapping disappeared and the patient is in good health.

Case II. Miss M. J., age 18 years. A routine blood test showed a Kolmer doubtful and a Kahn negative. On repetition, the Kolmer was positive and the Kahn negative. This girl came to me in tears under the impression that she had syphilis. Physical examination was completely negative for any symptoms of acquired or congenital syphilis; the history also was negative. At the time the tests had been taken the patient was just recovering from a "grippe-like" febrile respiratory infection. On re-examination by the same laboratory the blood serology gave negative results on both Kolmer and Kahn. One week later and again one month later these completely negative results were again obtained.

Comment: This patient, of course, did not have syphilis. The positive Kolmer reaction was false and probably due to the respiratory infection. Yet there are similar cases which have undergone treatment for syphilis.

Case III. Mr. T. M., age 60. This patient at infrequent intervals for a period of more than a year had "spells" during which he would momentarily lose consciousness. He would fall unless he sat down quickly. After the attacks he would feel perfectly well. Otherwise, his health was good. This patient was examined by several doctors who could find nothing but infected tonsils. The blood serology, taken several times, was negative for syphilis. The tonsils were removed with apparent benefit. After several months the attacks again returned. The patient was then referred to a neurologist who recommended examination of the spinal fluid. Two of the doctors previously consulted advised against having this done, giving the patient the impression that it was both dangerous and unnecessary. Others the patient spoke to advised "don't let them stick that needle in your back." Fortunately, this patient was not intimidated—many others would have been. The spinal fluid showed a
strongly positive Kolmer; cells, protein, and mastic were normal. A careful history elicited the fact that there had been fleeting, cramplike pains in the left calf which had occurred several times. On physical examination the second aortic sound was accentuated and of bell-like quality. These two symptoms had been previously overlooked.

**Diagnosis:** Neurosyphilis (beginning tabes), early aortitis.

**Comment:** After treatment for syphilis was started this patient had no further attacks. In the beginning, there were, on several occasions, slight premonitions that an attack might be impending; these also ceased. This case is cited for two reasons—first, many times the only serologic evidence of syphilis is found in the spinal fluid; and second, there are many, both patients and doctors, who have an unwarranted fear of spinal puncture. A spinal puncture properly done is not painful nor hazardous.

Case I is the patient who presents symptoms suggestive of syphilis with neglect to perform any serologic test. Case II is the problem of diagnosis in the asymptomatic nonsyphilitic patient when he may be treated for syphilis on the basis of inadequate serologic evidence. And case III, the failure to find syphilis in many cases unless the spinal fluid is examined.

Every physician in general practice and every physician in the various fields of specialty practice is confronted with these and many other problems in the diagnosis of syphilis every day. Yet not one of us, regardless of experience, is able or equipped to recognize all of the various clinical manifestations of this disease. Non monia possamus omnes (we cannot, all of us, do all things). Here, presenting itself, is a major problem in diagnosis to the end that all cases shall receive adequate treatment and that syphilis shall become an uncommon disease.

In the serologic diagnosis of syphilis there have been many changes and many improvements since the original Wassermann reaction. These developments have given us not a single test but many. While the old term "Wassermann reaction" may still be used in the general sense, meaning a serologic test for syphilis, the best method of expression is to give the tests their proper names which are the names of the authors, Kolmer, Kahn, Kline, etc. It is desirable to know what test or what several tests have been performed. Those tests which are acceptable and in common use in the United States are the Kolmer or Eagle complement fixation tests, and the Kahn, Kline, Hinton, or Eagle flocculation tests.

All of the tests are serologic reactions for the determination of the amount of reagin in the blood or spinal fluid. As nearly as can be explained, reagin is an antibody-like substance which is greatly increased in the disease syphilis but which may be increased under certain other conditions. Test for reagin depends upon two phenomena, the ability of reagin to combine with tissue lipoids (antigens) and fix complement—the complement fixation test, and its ability to combine with tissue lipoids to produce visible particulate suspension—the flocculation tests. The tests then are only different in their method of demonstrating the presence of reagin.
In obtaining specimens, not only is sterility important, but also chemical cleanliness. Syringes and needles must be boiled in clean water in a clean sterilizer. Alcohol sterilization is not permissible. Spinal fluid should not contain visible blood. If the blood is positive, traces of blood in the spinal fluid will give a positive reaction and lead to serious error in diagnosis. Specimens should be refrigerated until the time of examination. They will not spoil without refrigeration within any reasonable length of time, making it possible to send specimens to the laboratory through the mail.

A good laboratory should be selected. It is not necessary to discuss here the many factors which constitute a good laboratory. Briefly, a good laboratory should do at least two different tests on every specimen—one a complement fixation and the other a flocculation, and these should be done according to the method of the author of the test. Furthermore, it should qualify to perform the tests by regular comparison of its results with the results of the experts. State health department laboratories should qualify through the United States Serologic Conference. All the other laboratories should then be approved by their various State laboratories by submitting to periodic examination in which specimens are examined and the results compared. In all States where such machinery operates, the use of a State approved laboratory is recommended. You can then be assured of a sensitivity within 10 per cent and a specificity within 1 per cent of the results of the expert serologist.

Some years ago the method of reporting the reaction was negative, doubtful, one plus, two plus, three plus, and four plus. This led to some confusion, particularly in the minds of the laity who thought that they had more or less syphilis depending upon the degree of the reaction. The serologic test performed in the usual way is not quantitative and does not indicate the amount of reagin in the serum. There are, however, special quantitative techniques. Among doctors, there was always a difference of opinion as to the meaning of a one plus or a two plus reaction. Since this method of reporting could serve no useful purpose in the diagnosis of syphilis, a change was agreed upon to the use of the terms negative, doubtful, and positive.

Before entering further into the discussion of the interpretation of the tests, one point should be made clear. No test for syphilis can be evaluated except in terms of the patient. By that we mean that all of the facts of the case must be considered—a careful history, an analysis of the subjective symptoms, and physical examination.

**The Positive Reaction**

When a laboratory reports a reaction as positive, it means there is no doubt about the abnormality of the reaction. If the test has been performed in a good laboratory, technical error is not likely. Technical difficulties which occasionally arise usually produce weak reactions which are reported as doubtful reactions by the laboratory. Let us assume that both
a complement fixation and a flocculation test have been performed and that they are in agreement—both are positive. In all probability the patient has syphilis. On the other hand, what are the possibilities that he does not have syphilis? Diseases other than syphilis can produce sufficient reagin in the body fluids to obtain a positive serologic reaction—a biologic false positive reaction. The following diseases can and often do produce positive reactions: Yaws, pinta, leprosy, malaria, typhus, upper respiratory infections, infectious mononucleosis, vaccination, and serum treatment. The following diseases possibly can produce positive reactions: Febrile states, particularly active tuberculosis, rat bite fever, relapsing fever, and trypanosomiasis.

In former years, many conditions and diseases were suspected of giving a positive reaction. Among them were ingestion of alcohol, diabetes, menstruation, pregnancy, ether anesthesia, cream diet, etc. Modern serologic tests will not produce false results under these conditions.

In addition to the above conditions which can produce false positive reactions, approximately 1 person in 1,000 or perhaps as few as 1 person in 4,000 will show a temporary or a permanent false positive reaction. In the presence of definite and clear-cut symptoms of syphilis, there will be no difficulty in the interpretation of the positive reaction. However, in the absence of such symptoms it is imperative to differentiate between the positive reactions which are specific for syphilis, those which are technical false positive reactions, and those which are biologically false positive reactions.

The Doubtful Reaction

A doubtful serologic reaction for syphilis means exactly that. The reaction is too weak to be called positive, yet it is not frankly negative. Many of the false reactions discussed above will be found in this group. This reaction, under the older system of reporting, would have been a plus-minus, a one plus, or a two plus reaction. The reaction should be considered as suggestive of the possibility of syphilis. It is an indication for repetition of the rest and for further study of the patient.

The Negative Reaction

A negative serologic reaction does not exclude the possibility of syphilis. It is possible that a negative test may be a technical error. It must also be remembered that there are periods of the disease during which negative serologic reactions are obtained. In the presence of a suggestive history or clinical evidence of syphilis repetition of the test is called for; and, depending upon the circumstances, the test may be repeated many times, perhaps over a period of many months. Under some circumstances, a diagnosis of syphilis may be made without a positive serology.

Disagreement in Serologic Reactions

When two or more tests disagree, i.e., one negative and the other positive, repetition of the tests is indicated since an element of doubt is cast
upon the serologic report. While tests may vary because of technical factors, a report from a good laboratory is not likely to be completely negative by one technique and definitely positive by another due to technical error. Technical variations would more likely give results of negative and doubtful, or doubtful and positive.

Patients under treatment for syphilis quite commonly will show a disagreement of serologic reactions to the degree that a negative and positive report is obtained.

Among untreated patients known to have syphilis, disagreement of serologic reactions can occur. There is no satisfactory explanation for this condition. Greenbaum and Yagle\(^3\) found that eight out of fifty cases showed such a marked variation. The serums of these patients were examined on twelve consecutive days by the Kolmer and Kahn methods. It was demonstrated that in the individual case, untreated, considerable variation may occur. The value of performing more than one serologic test was clearly demonstrated by these experiments since one or the other test usually detected syphilis. In only two cases were both tests negative on the same day. The results also demonstrated the necessity for repetition of serologic examinations where syphilis is suspected.

When disagreement of two tests occurs and one is definitely positive, the history and clinical findings may warrant a diagnosis of syphilis; however, repeated serologic examinations will usually clarify the situation.

**Anticomplementary Sera**

In the performance of a complement fixation test, a control is used to detect anticomplementary activities. If the report is returned from the laboratory that the serum is anticomplementary, another specimen must be obtained.

**Presumptive Tests**

"Presumptive" tests, "exclusion" tests, or "screen" tests are serologic reactions performed by a supersensitive technique. The inference from the terminology used is that a positive test performed by a supersensitive technique is presumptive evidence of syphilis and that a negative test thus obtained would exclude such a possibility. This is apt to lead to a great deal of confusion. In the first place such tests are not diagnostic of syphilis, and secondly they do not exclude the possibility of syphilis. It is suggested, therefore, that these procedures be referred to as "screen" tests.

The chief function of such tests is the weeding out of individuals who may be unsatisfactory as donors for blood transfusion. Under this circumstance both the standard test and the screen test may be used; and if both are negative, the possibility of transfusion syphilis can be reduced to a minimum. The positive screen test should not be reported as a positive test for syphilis since it is too likely to be misinterpreted.

On receiving a positive or doubtful report on a screen test it is indicated to check the result several times by standard diagnostic tests, but
in the interpretation of the results disregard the results of the screen test.

**The Provocative Test**

In past years, the provocative serologic procedure has been used extensively in the diagnosis of syphilis. The indication for performance of such a test has been the patient who presented symptoms suggestive of, but not conclusively due to syphilis in whom negative or doubtful serologic results were obtained. In an attempt to obtain more conclusive evidence, a small dose of some antisyphilitic drug was given; and following this, blood or spinal fluid was examined once or repeatedly. The test was based on the assumption that in the presence of syphilis the amount of reagin would rise after the first injection of antisyphilitic drugs.

Usually the arsphenamines were used, perhaps 0.2 gm. of neoarsphenamine, and several days later blood would be taken for examination. In some instances the blood was examined a number of times during the first or even the second week after the dose of drug. Occasionally, the spinal fluid was examined. Bismuth was sometimes used in the same way and was always indicated where there was danger of the arsphenamine drug producing a serious Herxheimer reaction. It was thought that bismuth was not as likely to produce the provocative effect.

It is true that at times a negative or doubtful reaction would become more positive and a diagnosis could be more firmly established in suspected cases. However, in the light of present knowledge, this was probably nothing more than the variation in serologic reaction which occurs due to variations from day to day in the sensitivity of the tests.\(^4\,5\,6\) In other words, if the tests had been repeated without the administration of antisyphilitic drugs the same results would have been obtained.

At the present time the "provocative Wassermann" is rapidly falling into disuse. There are some, however, who insist that it is a sound procedure. It is certainly much more important in doubtful cases to examine the blood many times, and to send specimens to different laboratories before the administration of any treatment.

**Quantitative Serologic Tests or Serum Titre**

As is stated above, none of the tests for syphilis done in the usual way indicate the quantity of reagin present in the patient's serum. It is possible, however, to determine the titre or quantity of reagin in the patient's serum by performing any of the various tests on serial dilutions. By such procedures titres varying from one to hundreds or even thousands can be determined. To determine reagin titre, the work of a laboratory is greatly multiplied. This is seldom justified

These quantitative tests do not indicate that a particular infection is more or less serious, only that more or less reagin has been produced. A patient may have serious destructive pathology of the nervous system with a completely negative serology. These tests are of no value in the diagnosis of the average patient. It is interesting, and at times proves helpful
to follow the course of therapy by such tests. Quantitative tests are of
great value in investigative work, and are useful in the diagnosis of cer-
tain cases of congenital syphilis.

Kahn Verification Test

The fact that under certain conditions and even occasionally in normal
individuals serum may give a positive reaction in the absence of syphilis
leads to confusion and doubt in the diagnosis of asymptomatic syphilis.
Reuben Kahn¹ proposed a practical laboratory procedure for the detection
of biological false positive reactions. Serum is examined at 0°C and 37°C
as well as at the customary room temperature. A serum which shows
a stronger reaction at 37°C than at 0°C is showing the specific positive
reaction for syphilis. A serum which shows a stronger reaction at 0°C than
at 37°C is a false positive reaction.

More recently Kahn² has recommended a new verification technique
using salt solution. Three quantitative Kahn tests are performed; serum
1 is diluted with distilled water, serum 2 is diluted with 0.9 per cent solu-
tion of sodium chloride, and serum 3 is diluted with 2.5 per cent solution
of sodium chloride. A specific positive reaction for syphilis will show
the strongest reaction in serum 3, while a serum giving a biologic false
positive reaction will show its strongest reaction in test 1 and weakest in 3.

These new verification procedures are most important advances in
the serology of syphilis. They will probably become routine tests in the
diagnosis of asymptomatic syphilis removing the shadowing doubt which
always previously existed.

Examination of the Spinal Fluid

Spinal fluid examination is greatly neglected in the diagnosis and
treatment of syphilis. There are several reasons for this. Many physicians
are misinformed as to its value and do not seem to realize that, properly
done, it can be a painless office procedure. It is true that some patients
will have a post-puncture headache which may necessitate their lying flat
for several days, but this, too, is minimized by careful technique. Another
reason is that some patients are fearful of the procedure and imagine all
manners of dangers connected with "sticking needles into the spine."

If these tests were performed more often, many cases of early syphilis
of the nervous system would be recognized when the blood Wassermann
test is negative, and perhaps serious damage prevented. Such an examina-
tion is the only method for the diagnosis of asymptomatic neurosyphilis.

Contraindications to spinal tap are increased intracranial pressure,
serious or acute illness, extremes of age (the infant and the patient over
60 years of age), some cases of hypertension, pregnancy, and early syphilis
if less than six months of treatment have been given.

The indications for examination of the spinal fluid are many. At
some time, either before or during treatment, almost every syphilitic should
have such an examination. In the patient who has early syphilis, regard-
less of the results of the serology of the blood, the spinal fluid should be examined. Invasion of the spinal fluid is rather common and will require changes in the usual routine treatment if later damage is to be prevented. In late syphilis with but few exceptions spinal fluid examination should precede inauguration of therapy. It is important in the diagnosis of doubtful cases. Examination of the spinal fluid is often useful in planning therapy in cases of late syphilis. Its usefulness is not confined solely to the diagnosis and management of the patient who has symptoms of neurosyphilis. The knowledge gained may not alter the treatment plan in some cases, but it might in others.

*Spinal Wassermann:* Demonstration of the presence in the spinal fluid of syphilitic reagin by complement fixation or flocculation procedure is the only test which is specific for syphilis. The best serologic test for the spinal fluid is a complement fixation rather than a flocculation. It is preferable to perform the test on various amounts of fluid. Fluids positive to amounts of 0.2 cc. or less roughly indicate greater activity than fluids positive to 0.5 cc. to 1.0 cc. and negative in lesser amounts.

Certain other tests which indicate the degree of meningeal inflammation are of diagnostic and prognostic value, and are routine in the examination of the spinal fluid for syphilis. These tests are the cell count, some procedure for the estimation of protein (usually the globulin test), and a colloidal reaction (gold, benzoin, or mastic).

**Cell Count:** Less than 5 cells per cu. mm. is normal. More than 10 cells per cu. mm. is definitely abnormal. In neurosyphilis the cell count does not often rise very high—in the majority of cases not over 50. Cell counts of several hundred or even several thousand do occur. The higher cell counts indicate greater inflammatory activity. The highest cell counts occur in acute syphilitic meningitis and paresis. The cells present are principally lymphocytes.

**Globulin:** The Pandy globulin test is simple and commonly used for determination of an increase in the spinal fluid protein. The method is not a true quantitative test and, of course, is not a test of total protein. However, it is satisfactory. The globulin test is usually reported by such expression as normal amount, increased, greatly increased; or 0 for normal and one to four plus to indicate the degree of abnormality. Increase in globulin indicates inflammatory changes in the nervous system.

**Colloid Reaction:** Many still prefer the colloidal gold test, but due to technical difficulties the simpler colloidal mastic is often used. These tests are reported as a series of numbers varying from 0 to 5, or 0 to 3. If no numbers in the series are higher than 2, the test should not be considered as being abnormal. Series of numbers containing twos are borderline and threes indicate definite abnormality. The high numbers in the series may be in the center or at the beginning. In either position the meaning is much the same except that having higher numbers in the beginning is usually more serious and may indicate a paretic trend. The higher the numbers, the greater the degree of inflammation.
TABLE I
Suggestions for the Serologic Interpretation in Neurosyphilis

This tabular outline is not intended to be complete nor its opinions dogmatic. Much depends upon the character of the symptoms in the first column.

<table>
<thead>
<tr>
<th>History and Symptoms of Syphilis</th>
<th>Blood Wassermann</th>
<th>Spinal Fluid Examination</th>
<th>Neuro-Axis Involvement</th>
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<tr>
<td></td>
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<td>Spinal Wassermann</td>
<td>Cell Count</td>
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<td>rise</td>
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<td>moderate rise</td>
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<tr>
<td>Meningeal symptoms or asymptomatic</td>
<td>usually positive</td>
<td>highly positive</td>
<td>great rise</td>
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<td>negative</td>
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In the diagnosis of syphilis, four tests—(Wassermann, cell count, globulin, and colloidal gold or mastic)—should be done on every spinal fluid. This will give much more information than can be obtained from the Wassermann alone. Of course, it must be remembered that the cell count, globulin, and colloid tests indicate only irritation and are not diagnostic of syphilis. Meningitis from various causes, encephalitis, tumors of the brain and cord, and multiple sclerosis produce such abnormalities in the spinal fluid. However, if the spinal Wassermann is positive or if the patient is known to have syphilis even though the spinal Wassermann is negative, it is usually safe to assume that the patient has syphilis of the nervous system.

We have indicated above something of the meaning of the tests when considered individually. When considered collectively, various combinations of the four tests have various significances. And, of course, going beyond this, one must view from afar the whole kaleidoscopic panorama, piecing together all the facts of the case until a meaningful pattern evolves. (Table I)

It is impossible to discuss the interpretation of the serology in the diagnosis of syphilis without consideration of the disease itself. It must be remembered that while the tests will usually find syphilis if it is present, it is unwise to place too much reliance on a negative test and thereby fail to recognize seronegative syphilis. It is of utmost importance to carefully analyze the symptoms.

Primary Syphilis

Primary syphilis should never be diagnosed without laboratory confirmation. Furthermore, all lesions of the genitalia should be suspected. During the first few weeks after the appearance of a chancre, the serology is usually negative. Gradually, a positive serology develops. For this reason, a single serologic test at this stage does not rule out syphilis. Greater reliance should be placed on diagnosis by dark field examination. In any patient suspected of having the primary lesion of syphilis, the serology should be repeated weekly for several weeks, then monthly for three months, and study again made at six months. If the organism is identified in a genital lesion by dark field examination, a positive serology should not be waited for, but treatment started at once, since seronegative primary syphilis is the most curable stage of the disease. Doubtful reactions are very unlikely; they will be definitely negative or definitely positive. A doubtful serologic reaction will usually mean syphilis; but if the clinical manifestations are uncertain, the test should be repeated. In very early primary syphilis there may be disagreement in serologic tests, a positive flocculation and a negative complement fixation. This is due to the fact that the complement fixation is slower to become positive. This should offer no diagnostic difficulty, since within the first two weeks both tests become positive. Occasional cases are slow to become positive, as long as four or five weeks.
Secondary Syphilis

In secondary syphilis the serologic tests are virtually 100 per cent efficient. If a blood test is taken for all generalized skin eruptions, unless there is no doubt as to their character; in all cases presenting an unexplained prolonged fever, toxemia, or malaise syndrome; in all cases of sore throat which do not get well in two weeks; in cases of general lymphadenopathy; in cases of patchy loss of hair; in all cases with such rheumatic symptoms as vague bone pains and polyarticular arthralgia; and in all cases of iritis and neuroretinitis, then one will not fail to find secondary syphilis.

One might ask whether it is possible to have seronegative secondary syphilis. This is extremely rare. We have observed one such case in a patient who presented a clinically typical papular syphilid and who gave a history of exposure and development of a penile lesion. While seronegative syphilis can occur, this diagnosis should never be made without competent consultation.

Latent Syphilis

Early syphilis, the first two to four years of the disease, is a period of dissemination of the organisms to the various tissues and organs of the body through the circulating fluids, blood and lymph. It is a stage of spirochetemia; a period during which the immune reactions of the body are greatly stimulated. It is only natural to expect to find reagin in the blood in virtually all cases. The organisms disappear from the blood; but unless spontaneous recovery has occurred, they have invaded various tissues such as the liver, spleen, the walls of the blood vessels (particularly the aorta), and the nervous system. Now comes a period of latency—the patient is asymptomatic. The organisms in the various foci of invasion provoke no tissue reactions recognizable clinically to denote their presence. A state of local tissue immunity may be said to exist. This continues for a variable number of years or even throughout the life of the individual.

The patient's latent syphilis may never be discovered or perhaps at some time during his life he may have a routine serologic test for syphilis with a positive result. Now the physician has one of the most difficult decisions—the diagnosis of latent syphilis. This problem has become a common one since routine serologic tests are now so frequently done.

On making a diagnosis of latent syphilis, the patient, with but few exceptions, should undergo treatment—a therapy which is long, arduous, expensive, and dangerous. Unless from the lowest social strata, the patient is subjected to a great amount of worry and mental anguish which the best psychological approach has difficulty combating.

It is hardly necessary to say that there must be no uncertainty in the mind of either physician or the patient in reaching the conclusion that the patient has syphilis. After starting treatment one is never able properly to retrace the steps necessary in the diagnosis of latent syphilis. How horrible to be confronted by the patient who has been so diagnosed and treated if he later comes to the belief that there may have been a doubt.
History. The first step when confronted by a doubtful or positive serologic test is to take a careful and directive history. This will involve questioning regarding any previous serology or treatment. If the result of previous serologic examination is not known, it should be ascertained. Previous symptomatology of syphilis should be searched for. The obstetrical history of women and the history of family health should be recorded. It is also quite important to obtain history regarding diseases which may give rise to biologic false reactions.

Physical Examination. The second step is a careful physical examination searching for possible clinical activity which has been overlooked. In many such cases, cardiovascular or neurological symptoms will be present. These patients, then, have active or symptomatic syphilis which passed unrecognized. Failure to recognize an existing pathology may lead to serious consequences in the future management and treatment. The physical examination should aim to disclose more than the symptomatology of syphilis—it is necessary to rule out the diseases which produce false positive reactions. Under certain conditions of history and physical findings, the examination may include investigation for malaria, infectious mononucleosis, etc.

Serologic Follow Up. The next step is a serologic study of the patient and all possible contacts. A positive serologic report on a contact might lend weight to the diagnosis. More important than all else is the repetition of serologic tests. Under some circumstances of history, two or three positive tests may be adequate evidence of syphilis. It is frequently necessary to perform a series of blood tests extending over a period of weeks or months. The same and other laboratories should be used. If the patient has recently had a disease or condition known to produce false reactions, sufficient time should elapse before positive reports are considered specific. This is usually a matter of weeks; it is wise, however, to continue serologic study under such a circumstance for a period of months. The Kahn verification test should be done to determine if the reaction is a biologic false positive or a specific (syphilitic) positive reaction.

If three positive tests are obtained from good laboratories, if there is agreement in both flocculation and complement fixation procedures, and if none of the conditions producing false reactions are known to exist, the patient probably has syphilis. On the other hand, it seems well established that a normal, healthy, nonsyphilitic can have a positive reaction. This is, of course, a rarity. If one of the tests has been a Kahn verification procedure, this rare possibility can be excluded.

Cerebrospinal Fluid. The next step in the diagnosis of latent syphilis is examination of the spinal fluid. If there is a suspicion that the infection is recent, and the diagnosis is early latent syphilis (two to four years from the time of exposure), such an examination should be withheld until at least six months of treatment has been given. Positive findings in the spinal fluid may be helpful in strengthening a doubtful diagnosis. Equally important is information necessary in planning therapy.
Another aid in the diagnosis of some doubtful cases is roentgen examination of the aorta for cardiovascular syphilis.

**Late Syphilis**

During the first few years after the human body has been invaded by the organism the blood serology is most efficient in diagnosis. As years pass, the incidence of positive serology continues to fall. Regardless of this drop in effectiveness, serologic tests will diagnose the various clinical manifestations of late syphilis with great regularity. Examination of the spinal fluid has now (late syphilis) acquired greater importance in diagnosis. The weight of clinical evidence may be great enough that in spite of negative serology of the blood and spinal fluid a diagnosis of syphilis can be made. Under other circumstances of negative serology of the blood and spinal fluid, the clinical evidence may not be sufficient to warrant a diagnosis. In some of these selected cases, the so-called therapeutic test may be important in differential diagnosis. However, the greatest value of the therapeutic test lies in the differentiation of symptoms which may be due to syphilis or to some other disease in the individual known to have syphilis, rather than in the individual who has a completely negative history and serology.

Many are the problems of serologic interpretation in the diagnosis of late syphilis. Any adequate consideration of these problems would involve such a thorough discussion of all the pathologies, their symptoms, and differential diagnosis as only could be contained in a sizable volume. Again, it must be emphasized that no diagnosis should be made except in the face of incontrovertible proof. There are now more and more occasions when one is unable to depend upon the serologic tests to furnish that proof. Several examples may be used for purpose of illustration. The patient with neurological symptoms may have a negative blood test and even a negative spinal fluid and yet have neurosyphilis, i. e., when the diagnosis of tabes dorsalis can be clearly established on clinical grounds. An example of the reverse of this situation is the differential diagnosis between neoplasm and syphilis. A positive serologic test for syphilis can only mean that the patient has syphilis and is never proof that a lesion suspected of being a neoplasm is syphilitic. A biopsy is the method of differentiating these two lesions.

Modern serologic tests are much more sensitive than older ones, and it is necessary to revise our knowledge as to the incidence of positive blood serology in late syphilis. Becker and Obermayer give the following figures on the incidence of positive serology in late syphilis:
Table II

Percentage Incidence of Positive Serology in Late Syphilis

| Late latent | men 90 — women 50 - 80 |
| Cardiovascular | 80 - 96 |
| Osseous | 80 - 90 |
| Neurosyphilis: | |
| Early latent | 85 - 100 |
| Late latent | 70 - 90 |
| Tabes dorsalis | 80 - 85 |
| General paresis | 98 - 100 |
| Prenatal | 40 - 95 |

Congenital Syphilis

Serologic tests on blood obtained from the umbilical cord at the time of birth are of little or no diagnostic value. The reason for this is that reagin from the maternal blood passes freely through the placenta to the child. A positive cord Wassermann may be obtained in a child born of a syphilitic mother and the child may be nonsyphilitic. And the opposite of this, a child with a negative cord Wassermann may later prove to have syphilis. Pathologic examination of the placenta has also been discarded as offering the same confusion in diagnosis as the cord Wassermann. The only positive proof of syphilis at the time of birth of a normal appearing child is a positive dark field examination from the wall of the umbilical vein. This test has not been commonly used but certainly should prove well worth the effort when a child is born of a mother known to have syphilis.

X-ray study of the infant’s long bones has been recommended for the early recognition of congenital syphilis. A great amount of investigative work has been done, and under some circumstances the procedure may prove useful. But as yet nothing has replaced thorough serologic study and clinical observation.

As in the case of the cord Wassermann, blood obtained from the child by venipuncture may also be positive in a newborn child who does not have syphilis. Furthermore, the child’s blood may remain positive for eight or nine weeks. The newborn child should be examined frequently for clinical evidence of syphilis. We usually examine the blood at four weeks and again at eight weeks; but if the child is well and shows no evidence of syphilis, we withhold treatment for another month. At three months of age, if the serum is positive, a diagnosis of syphilis is made regardless of negative clinical findings. It is of utmost importance to start treatment at once if symptoms should appear during this waiting period.

Studies have been made of reagin titre in the diagnosis of congenital syphilis. At the time of birth, if the reagin titre of the mother and child are compared, it is often found that the child who is syphilitic will have a much higher titre. Further serologic studies of the child’s blood will
show in the weeks which follow a rapid fall in serum titre if the child is non-syphilitic and a rapid rise, often after a preliminary drop, in the child who is syphilitic. The practical value of titre estimation is rather doubtful. Diagnosis by such procedure can hardly be arrived at much sooner, and it seems well established that the child who is positive at the end of three months has syphilis regardless of other findings, and that the converse of this is probably true, that the child who is negative at the end of three months does not have syphilis. We usually recheck the blood at six months and again at one year.

It must be remembered that a syphilitic child may have a negative test at birth or at four weeks; it will, however, usually become positive at eight weeks and certainly should be positive at three months.

Summary

Syphilis is a prevalent disease and the serologic tests should be used freely.

A "high index of suspicion" should be maintained. This can only come from an adequate knowledge of the disease and its varied symptomatology.

Treatment should not be started with an uncertain diagnosis. It is usually possible to be sure if the problem is studied carefully.

Serology should be interpreted in terms of symptomatology. No attempt to discuss the clinical manifestations of this disease has been made in this paper.

References

RADIOLOGICAL CONSIDERATION OF TUMORS OF BONE

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Bone tumors offer many and varied radiographic characteristics; but they do possess certain peculiarities which make them, in many instances, readily defined and properly appraised at film examination. It goes without saying that pathologies involving the skeleton may, and not infrequently do call forth every scientific means of investigation at the disposal of the orthopedist and radiologist before an accurate diagnosis can be established and suitable treatment instituted. That the diagnosis and differentiation of bone tumors requires exacting study may be readily inferred by repeating Kalodny’s statement that “to read and interpret correctly a roentgenogram of a bone tumor is an art acquired only with wide experience, combined with a thorough knowledge of gross pathology.” By implication, too, it may be reasoned that the treatment of bone neoplasms likewise requires more than ordinary training and experience. In other words, the subject under discussion is one commanding the collaborative interests and actions of the orthopedist and radiologist.

The approach to the diagnosis and treatment of bone tumors implies the necessity for a detailed case history, a thorough and complete physical examination, adequate laboratory investigation, roentgenological examination, and biopsy whenever indicated. It is the purpose of this paper to deal briefly with the radiographic findings observed in some of the bone tumors met in hospital practice, and to refer to certain findings which contribute to the diagnosis and differentiation of these tumors.

For purposes of presentation, bone neoplasms have been divided into two groups. In the first group have been placed those tumors which are primary, having their origin in bone. The second group includes the metastatic or secondary lesions.

Tumors Originating in Bone

Osteomas: True osteomas are tumors composed entirely of osseous tissue. They are productive lesions and most often have their origin in the cortical substance. Osteomas are found to vary in shape, size, and density as revealed at x-ray examination. Osteomas may contain cancellous bone, medullary substance, or be composed of dense bone giving the tumor an eburnated appearance. True osteomas are found most commonly to involve the femur, tibia, and humerus, and occasionally one encounters a true osteoma in the frontal or maxillary sinuses. Osteomas obey the laws of benign tumors and are productive of symptoms only insofar as their presence produce mechanical irritation and pressure in the overlying soft tissues and vessels. An osteoma located close to a joint may limit articular mobility.
Osteochondromas: (Figures 1 and 2) are benign tumors which contain cartilage, and they are common in occurrence. These tumors are usually found to arise from the site of a tendon attachment, which undoubtedly accounts for the cartilaginous elements found in them. Primitive cartilage cells are retained in the base of the tendons, and under suitable conditions they proliferate and grow. The resulting neoplastic change is one involving both osseous and cartilaginous structures.

Osteochondromas exhibit roentgenologic characteristics which are quite typical. They possess an osseous base or pedicle which arises from an intact cortex. The limiting margin of the tumor, though irregular, is sharply outlined and demarcated. The tumor possesses areas of spotty calcification and also zones of radio translucency due to the contained cartilaginous elements. The growth of the tumor takes direction in the line of muscle pull.

Osteochondromas may at times become malignant, undergoing sarcomatous degeneration.

Multiple Exostoses: Multiple or benign exostoses are met with in the form of an hereditary deforming chondrodysplasia. There is usually an associated familial or hereditary factor in most cases of this sort. (Figures 3 and 4.) The exostoses are seen to spring from many bones, including the femur, tibia, radius, ulna, humerus, and ilium, to produce deformity, and to be in position where they could interfere with function of the involved parts.

There are certain radiographic findings which characterize multiple exostoses. The tumors possess a pedicle, the lesions are multiple, the bones of the leg and forearm are bent and malformed, and the exostoses point away from the nearest joint.

These tumors may undergo malignant degeneration just as in the case of osteochondromas.

Chondromas constitute another type of benign cartilage growth; but instead of arising from a peripheral site, they are located within the bone. These tumors develop and grow slowly; and, conforming to the pattern of benign lesions, they expand, but do not destroy the cortex. The cortex may break under the influence of pressure from within, but there is no evidence of soft tissue invasion when this takes place. The involved tumor-bearing area may show fine striated or trabecular markings, and calcareous deposits of increased radio density may also be seen.

These tumors occur commonly in the phalanges of both upper and lower extremities. They are also occasionally found to involve the sternum and long bones, and in these latter locations are almost invariably malignant. In the past five years we have observed three cases of chondroma of the sternum. In each case, biopsy proved the lesion to be a chondrosarcoma.

Primary Chondrosarcomas (figures 5 and 6) are extremely malignant neoplasms which usually have their point of origin at the end of the shaft of a long bone, arising from the site of a tendon insertion. They develop in residual embryonal cartilage, grow rapidly, and tend to invade and
destroy both cortex and medullary substance. Early chondrosarcomas show no roentgen evidence of cortical or medullary destruction. There is a soft tissue mass noted both at clinical and radiographic study, and in the soft parts close to the bone there may be seen a few fine calcified spicules which radiate outward from the superficial limits of the bone.
These tumors are usually found in patients from fourteen to twenty years of age, and they are rapidly fatal. The earliest clinical manifestation of chondrosarcoma is pain which becomes progressively more severe. The presence of fever and mild leucocystosis may also be noted. These findings may suggest an inflammatory rather than a malignant bone tumor.
Osteogenic Sarcomas (figures 7, 8, 9, 10) are malignant tumors which result from degenerative changes arising in the osteogenetic parts of bone. Osteogenic sarcoma occurs in two forms, (a) the osteoblastic or sclerosing type, and (b) the osteolytic type.

The osteoblastic or sclerosing form of osteogenic sarcoma most often
occurs during puberty and up to the twenty-fifth year. Its roentgen characteristics are well known, and in its typical form shows the changes so frequently described in the text-book presentation of osteogenic sarcoma. In its earliest stage of development this tumor produces an increase in density of the medullary bone, usually at the metaphyseal area, and favoring the diaphyseal or shaft side. The periosteum is slightly roughened and irregular. As the tumor develops, the x-ray findings are apt to indicate the typical characteristics of the lesion, with numerous calcified spicules and fine plaques of new bone arranged at right angles to the cortex. This tumor produces bone, but there will be evidence of both cortical and medullary destruction in the advanced stages of the disease.

The osteolytic type of osteogenic sarcoma is a destructive and extremely malignant tumor. It is most usually found in young individuals, and like the osteoblastic osteogenic sarcoma and chondrosarcoma occurs most frequently during the period of maximum bone growth and development. Osteolytic osteogenic sarcoma arises in the medullary bone, probably as an endosteal lesion, and like the osteoblastic form is located in the metaphyseal zone. This tumor produces medullary destruction with early violation of the cortex, leading to infiltration and invasion of the adjacent soft parts. It is markedly vascular, and at times the tumor mass may fluctuate or pulsate. The vascular features of the tumor account for its being referred to by many older writers as bone aneurysm.

The clinical aspects of osteolytic osteogenic sarcoma are pain, loss of function, and swelling of the soft tissues over the end of the bone, all of which may have followed a seemingly slight injury. Not infrequently the temperature may be found to be slightly elevated (100°-101°) accompanied by some alteration in the blood count, with a mild leucocytosis (10,000-12,000). These findings may lead to a clinical diagnosis of osteomyelitis and result in surgical treatment being carried out. However, at surgical exposure the operator encounters blood and hemorrhage and not pus. If cultures are not made, and tissue is not taken for immediate frozen section, it is unlikely that a true diagnosis of the condition will be made until a time too late for any form of treatment to be employed which will be of benefit to the patient.

**Bone Cysts** [figure 11] are destructive lesions which are benign in nature and which rarely produce symptoms. Typically, bone cysts are found to affect the end of the shaft or diaphysis close to or abutting the metaphysis. Cysts of bone are frequently found in the proximal portion of the humerus, femur, or tibia. They occur chiefly during the early age periods, usually prior to puberty, but may be encountered in older patients where their presence becomes known as a result of pathologic fracture. Cysts produce a more or less fusiform expansion of bone, thinning, but not breaking the cortex. If fracture occurs through a cystic lesion, some productive bone reaction will usually be found at x-ray examination. This may be accounted for on the basis of bone repair.

Bone cyst is to be differentiated from the localized form of osteo-
myelitis (Brodie’s abscess). The latter condition, being of pyogenic origin and usually chronic in nature, will, at x-ray examination, show a limiting margin of bone condensation with some periosteal thickening but no expansion of bone. Brodie’s abscess as a rule will produce local pain and tenderness; whereas, in bone cyst, these findings are absent. If explored or treated surgically, positive cultures will be obtained from the abscess and negative bacterial findings will prevail in the case of bone cyst. Tissue removed at operation if subjected to microscopic examination, will settle
any question as to the character of the lesion. Bone cyst is to be further
differentiated radiographically from chondroma and myeloma.

Osteosis Fibrosa (Von Recklinghausen’s disease) is a disease of the
bone characterized by cystic change, which tends to involve the major
portion of one or more bones. It is usually encountered as a multiple
lesion. In its typical multiple form, the bones give evidence of a malacic
tendency and become bent and distorted. X-ray examination reveals the
presence of multiple cystic defects in the expanded and deformed bones.
As a rule the cortex is thinned but preserved, and the trabecular archi-
tecture is generally disturbed and altered, being poorly defined in and
about the cystic zones.

It is now generally accepted that osteosis fibrosa is due to parathyroid-
ism. Tumor or hyperplasia of the parathyroid glands resulting in dysfunc-
tion of these structures affects the calcium and phosphorous levels of the
blood stream through an overproduction of parathormone, which in turn
results in an extraction of calcium from its fixed location in the bony
skeleton. In the presence of generalized or multiple osteotic changes,
study of the blood chemistry is always indicated.

Giant Cell Tumor (osteoclastoma) is a benign, destructive, and cyst-
like tumor which most often involves the epiphyseal region of a bone.
(Figures 12, 13.) These lesions are found in adults and most commonly
are encountered in the distal end of the femur or proximal portion of the
tibia. Giant cell tumor involves the central portion of the bone, usually
favoring an asymmetrical location. Its radiographic appearances are, as a
rule, quite typical. The cortex is thinned and expanded, though not broken
through except in the case of a pathologic fracture. Within the tumor,
coarse trabeculae may be demonstrated, which become increasingly less
prominent as the tumor enlarges. Multiple radiotranslucent zones are
present, giving the growth a loculated appearance. The symptoms present
in those cases seen by the writer were pain and disability of the part,
accompanied by swelling of the soft tissues.

The treatment of giant cell tumor may be carried out by surgical
excision or curettage followed by chemical cauterization, or the tumor
may be treated entirely by high voltage irradiation. This latter form of
treatment is recommended when the tumor is located in a weight-bearing
area and abuts on joint cartilage. Irradiation should also be the method
of choice in treating giant cell tumors of the skull and vertebrae.

During the past three years the writer has encountered several cases
of giant cell tumors which have displayed rapid development and wide-
spread osteolytic proportions, even to the invasion of surrounding soft
parts. In at least three instances, attempts to explore, resect, or even
curette these tumors by direct surgical approach met with failure because
of the degree of vascularity of the tumor resulting in profound hemor-
rhage. The tissue secured in each case, though scant in amount, enabled
the pathologist to interpret the tumor as giant cell variant of the spindle-
cell order. Two of these cases operated in our hospital established the
giant cell variant in the pubic bone in one instance, and in the cervical spine in the other. Both cases were subjected to irradiation and responded satisfactorily.

Malignant giant cell tumors have been reported in the literature, the tumors displaying metastases and resulting in death of the patient. In
none of the cases referred to by Geschickter was there found in the pulmonary metastases any microscopic evidence of typical giant cell tumor. In every instance the metastatic nodules showed histological findings indicative of osteogenic sarcoma. One may therefore suppose that either an osteogenic sarcoma developed as a complication of the benign giant cell lesion, or that an error in evaluation permitted the original diagnosis to favor a benign tumor rather than that which really existed, namely, osteogenic sarcoma.

*Ewing's Tumor* (Ewing sarcoma, endothelial myeloma) is a malignant neoplasm, with a histogenic background which is not as yet quite clear. (Figure 14.) Recent investigations suggest that it has its origin in the lymphatic endothelium of bone. When this tumor involves a long bone, it produces quite a typical radiographic picture, though one which is, unfortunately, easily mistaken for osteomyelitis. At x-ray examination, Ewing's tumor is seen to produce early medullary condensation with periosteal reaction indicated by the presence of thin layers of bone laid down parallel to the shaft. This is followed by bone destruction, resulting in elevation and splitting of the periosteum and giving the so-called "onion-peel" appearance. The cortical bone shows areas of increased and decreased bone density, resulting from destructive and replacement changes in the compact bone tissue.

Ewing's tumor occurs in early life. Its clinical course is marked by a gradual onset of mild pain located in the region of one bone. There are usually intermittent attacks of fever with no appreciable change in the
blood count. These findings are followed or accompanied by the development of a tumor mass, which, according to Ewing, "may increase rapidly for a short period and then partly subside, or the growth may be rapid, and progressive."

This tumor is usually quite radiosensitive and will respond promptly
to irradiation in a high percentage of cases. This response will serve to
differentiate the lesion from osteomyelitis which is not readily influenced
by irradiation.

The differentiation of Ewing's tumor from osteomyelitis may be aided
by giving consideration to the following points:

<table>
<thead>
<tr>
<th>Osteomyelitis</th>
<th>Ewing's Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>High, 102° - 105°</td>
<td>Temperature</td>
</tr>
<tr>
<td>Polymorphonuclear cells increased.</td>
<td>Blood count</td>
</tr>
<tr>
<td>Early bone changes questionable or not present. Periosteum intact until late.</td>
<td>Radiographic findings</td>
</tr>
<tr>
<td>Produces no change.</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td></td>
<td>Biopsy</td>
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</table>

Ewing's tumor offers a bad prognosis. The fact that in most instances
this tumor responds to irradiation, makes possible its being held in check
for a considerable time. Resection and amputation have not proven to be
successful means for coping with this tumor. The great tendency of
Ewing's tumor to recur, together with its ability to metastasize, inevitably
leads to a fatal ending.

Tumors Originating Outside of Bone

Fibrosarcoma and Neurosarcoma are soft parts tumors, which may
invade bone from without or may produce a smooth marginal osseous
defect due to pressure.

Fibrosarcomas are tumors of low grade malignancy. They are com­
posed of fibrous tissue elements and frequently have their origin in fascia.
At x-ray examination the neoplastic changes are greatest in the soft tissues,
with a tumor mass located outside of the bone. The periosteal or cortical
bone may show a productive reaction with little or no bone destruction,
or the tumor may destroy the superficial osseous structure without visible
periosteal change.

Neurosarcomas are highly malignant tumors which arise outside of
bone; but, like the periosteal fibrosarcomas, they infiltrate and invade bone
from without. Neurosarcomas usually progress and grow rapidly, and
but few cases are cured under any system of treatment.
Both fibrosarcoma and neurosarcoma are tumors which offer little in the way of characteristic radiological appearance, and diagnosis in both instances is made with great difficulty even when biopsy is carried out.

The second group of tumors originating outside of bone to be given consideration are those which involve bone by virtue of metastasis. Tumors which most often metastasize to bone are those which originate in the breast, prostate, kidney, and thyroid.

Breast carcinoma (figures 15 and 16) very frequently metastasizes to the bony skeleton. The bony pelvis, spine, and skull are commonly the sites of metastatic carcinoma originating in the breast. The humerus and femur are also frequent locations for the metastatic breast lesion. It is rare to find metastases below the elbow and knee in this disease.

The usual breast carcinoma tending to metastasize to bone does so by producing multiple lesions characterized chiefly by their destructive manifestations. At times, bone production may be indicated at x-ray examination, but almost always this change is overbalanced by the degree of bone destruction present. The multiple metastatic lesions involve and destroy both central and marginal bone with an irregular contour resulting, or the marginal lesion may gradually fade out and blend with the normal osseous structure. When the spine is involved, vertebral destruction with collapse of the body is a common finding. The compression deformity
Osteal carcinoma. Multiple osteolytic lesions involving the cranial bones. Metastatic mammary carcinoma. Characterized by multiple areas of bone lysis. An example of metastasis by blood stream.

Fig. 15. Osteal carcinoma. Metastatic mammary carcinoma. Characterized by multiple areas of bone lysis. An example of metastasis by blood stream.

Fig. 16. Osteal carcinoma. Multiple osteolytic lesions involving the cranial bones. Metastatic mammary carcinoma.

of the vertebral body suggests a pathologic fracture. When metastases occur in the extremities, pathologic fracture is a rather frequent finding and sometimes is the first indication of existing osteal carcinoma.

Multiple Myeloma is a neoplastic lesion of bone which may be most easily mistaken for and confused with metastatic carcinoma. Myelomas arise from cells located in the bone marrow, and they produce a destructive action on bones which results in a rather characteristic roentgen picture. These lesions are multiple and have a smooth, rounded, and punched-
Osteal carcinoma. Metastatic lesion involving the shaft of the humerus. Carcinoma of the kidney was the primary tumor. The metastatic focus was in single form and was located to the anatomic level of the nutrient artery.

Osteal carcinoma. Metastasis from carcinoma of the kidney. Destructive lesion involving the second rib on the right side.

out appearance. Multiple bones are involved, and the lesions are purely destructive. The skull, ribs, sternum, clavicles, spine, and pelvis are the parts most often involved. Multiple myeloma is a disease often seen in adult life, occurring frequently during the middle age period. The dominating symptom is pain, which, as the disease progresses, becomes
severe and unbearable. Weight loss and cachexia are constant findings, while spinal cord symptoms commonly result from compression of the cord following widespread vertebral involvement. The diagnosis of multiple myeloma is materially aided by the demonstration of Bence-Jones bodies in the urine; the test being positive in approximately 65 per cent of all cases.

*Carcinoma of the Prostate* frequently metastasizes to bone and most often demonstrates its metastatic characteristics in the lumbar spine, pelvis, and femora. This lesion differs from osteal carcinoma secondary to breast cancer in that it results in a desmoplastic change in bone, which at x-ray study impresses one as being a process of a productive rather than destructive nature.

The involved bones take on an osteitic appearance. They become increased in radiodensity and appear to be coarsely granular in structure and composition. Osteal carcinoma of prostatic origin is quite apt to be confused with Paget's disease of bone. The trabeculae or striae are visible and tend to be preserved. Paget's disease, unlike the metastatic prostatic lesion, results in bowing of the long bones, the tibiae being frequently affected. The tibia is not involved in metastatic carcinoma of the prostate, since this lesion has not been found to produce secondary involvement below the knee.

*Malignant Nephroma* (papillary carcinoma or so-called hypernephroma) often metastasizes to bone, with the metastatic process occurring as a single or solitary lesion. (Figures 17 and 18.) There is found at x-ray examination an area of bone destruction involving the shaft of the humerus or femur at a site corresponding to the anatomic location of the nutrient foramen. Radiographic examination of other parts of the skeleton reveals multiple metastatic foci.

In concluding this paper, we wish to briefly review the typical differential characteristics of benign and malignant neoplasms of bone, as they are demonstrated at x-ray examinations. In benign tumors of bone, the limiting contour and margin of the involved part is maintained. The cortex of the bone may be expanded and thinned, but it is not destroyed. Benign tumors do not invade or infiltrate the surrounding and adjacent soft tissues, and they do not metastasize. Malignant tumors of bone are destructive in nature. They break through and destroy the cortex. They display great tendency to invade and infiltrate surrounding parts, and to metastasize to other portions of the body. The malignant lesions usually create an irregular outline of bone in contradistinction to the smooth contour characterizing the benign lesion.
BONE TUMORS

References
