BIOLOGICALLY FALSE POSITIVE REACTIONS TO SEROLOGICAL TESTS FOR SYPHILIS

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SYNOPSIS

The frequency of biologically false positive reactions to serological tests for syphilis depends on a number of factors, including the individual immunological response, the number and type of serological tests performed, and the stage of the disease producing such reactions; the relative importance of such factors is discussed. The author also considers in detail the diseases or conditions giving rise to acute or chronic biologically false positive reactions.

A variety of verification tests exists for differentiating the true syphilitic reaction from the biologically false positive reaction, but none is so accurate as the Treponema pallidum immobilization and immune adherence tests, which the author considers should be used when others have proved inconclusive. In the final section of his paper, he indicates the steps to be followed in attempting to distinguish between latent syphilis and biologically false positive reactions in persons with positive serological tests but no anamnestic or clinical evidence of syphilis.

The term "biologically false positive reaction" is that used to denote the reactivity with lipoidal antigens and cardiolipin antigens of sera from patients who do not have syphilis or other treponematoses. A recently suggested name for such reactive sera in serological tests for syphilis is "reactive non-treponematic sera". In view of the universally recognized and accepted use of the former terminology the expression, "biologically false positive reaction" will be exclusively employed in this communication.

The increased attention directed to the subject of biologically false positive reactions is warranted in view of the relative increase in the frequency of such reactions. The decline in the number of cases of syphilis, as a result of the advent of penicillin and other treponemical antibiotics, has resulted in fewer true syphilitic reactions with a resultant increase in the proportion of biologically false positive reactions. The recent developments and improvements in the means of differentiating true from biologically
false positive reactions has lent further importance to this subject. Foremost in this connexion are the specific procedures discovered by Nelson and his co-workers in the form of the *Treponema pallidum* immobilization test and immune-adherence reaction, both of which are discussed in other papers in this *Bulletin*. The fact that such verification procedures are available has stimulated clinicians to look for and set apart these non-syphilitic reactions from those of true syphilis. Whereas in former years many individuals with non-specific reactions were erroneously treated for syphilis, at the present time more and more physicians are properly diagnosing these cases. Finally, it is being recognized that one cannot casually dismiss from observation the patient with a long-standing biologically false positive reaction. Recent workers have shown that many of these individuals, when thoroughly investigated, have clinical and laboratory evidence of potentially serious systemic disease.

No more is known of the actual mechanism causing biologically false positive reactions than is known of the mechanism of the true syphilitic reaction. The apparent anomaly of lipoidal antigen extracts reacting with syphilitic serum has always been a source of considerable vexation to the immunologist.

The theory that alterations in the serum protein fractions may be an etiological factor in biologically false positive reactions has never been substantiated. Whereas such diseases as lupus erythematosus and lymphogranuloma venereum are associated with hyperglobulinaemia and biologically false positive reactions, other diseases such as multiple myeloma show hyperglobulinaemia without biologically false positive reactions. Moreover, in lupus erythematosus there is no correlation whatsoever between the frequency of biologically false positive reactions and hyperglobulinaemia. Many cases show false positive reactions with normal protein values, whereas others with altered serum protein values do not manifest biologically false positive reactions. In a study from Central America of the relationship between biologically false positive reactions and the protein content of serum, Stout and her colleagues were unable to find any significant correlation.

**Frequency**

The frequency of biologically false positive reactions in any disease entity is dependent upon a variety of factors:

(1) **Individual immunological response**

There are certain individuals whose immunological mechanisms are so labile as to be altered by a variety of noxious stimuli. In these serological reactors any one of a variety of diseases may result in the production of
BIOLOGICALLY FALSE POSITIVE REACTIONS

biologically false positive reactions. Upper respiratory infections, virus pneumonia, smallpox vaccinations, etc., easily precipitate these individuals into serological reactivity. The greater the number of such serological reactors, the greater the frequency of biologically false positive reactions in any given disease entity.

(2) Type of serological test

As a general rule the cruder the lipoidal antigen, the greater the frequency of biologically false positive reactions. This is remarkably demonstrated in connexion with malaria. Employing the Kahn reaction one obtains as high as 80% false positive reactions with sera of patients with acute attacks of malaria. Employing the highly purified phospholipid cardiolipin in antigenic emulsions this rate approaches zero. (With the Venereal Disease Research Laboratory (VDRL) slide test, some 4% reactors are found among the same sera.)

(3) Number of tests

The greater the number of serological tests for syphilis performed on any one specimen, the greater will be the frequency of biologically false positive reactions.

(4) Frequency of tests

The more frequently the serological tests for syphilis are performed during the course of any disease process, the greater will be the frequency of biologically false positive reactions.

(5) Stage of disease

In certain disease groups the frequency of biologically false positive reactions varies with the stage of the disease. For example, lepromatous leprosy results in greater numbers of biologically false positive reactions than does tuberculoid leprosy. The type of reaction to smallpox vaccination governs the frequency of resultant biologically false positive reactions to tests for syphilis. Individuals with the vaccinia or non-immune response show a greater frequency of biologically false positive reactions than do those with the accelerated or immune responses. The greatest reaction in such persons appears within 8-14 days after vaccination.

All the previously enumerated factors and others must be evaluated in any study of the frequency of biologically false positive reactions in any disease entity. Unless these factors are considered, comparative incidence studies are of little value.

In a report culled from their vast experience, Moore & Mohr recently compiled the following list of non-syphilitic diseases capable of producing biologically false positive reactions:
### Approximate percentage of biologically false positive reactions

#### Infections

<table>
<thead>
<tr>
<th>Category</th>
<th>Disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Bacterial</td>
<td>Leprosy</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis, advanced</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Pneumonia</td>
<td>2-5</td>
</tr>
<tr>
<td></td>
<td>Pneumonia, pneumococcal</td>
<td>2-5</td>
</tr>
<tr>
<td></td>
<td>Subacute bacterial endocarditis</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Chancroid</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Scarlatina</td>
<td>5</td>
</tr>
<tr>
<td>(b) Spirochaetal</td>
<td>Leptospirosis</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Relapsing fever</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Rat-bite fever</td>
<td>20</td>
</tr>
<tr>
<td>(c) Plasmodial</td>
<td>Malaria</td>
<td>100</td>
</tr>
<tr>
<td>(d) Rickettsial</td>
<td>Typhus</td>
<td>20</td>
</tr>
<tr>
<td>(e) Protozoal</td>
<td>Trypanosomiasis</td>
<td>10</td>
</tr>
<tr>
<td>(f) Viral</td>
<td>Vaccinia</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Pneumonia, &quot;atypical&quot;</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Measles</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Chickenpox</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Lymphogranuloma venereum</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Infectious hepatitis</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Infectious mononucleosis</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Common cold</td>
<td>? (low)</td>
</tr>
</tbody>
</table>

#### Non-infectious diseases or conditions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lupus erythematosus</td>
<td>20</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>5</td>
</tr>
<tr>
<td>Blood loss, repeated</td>
<td>? (low)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>? (low)</td>
</tr>
</tbody>
</table>

The approximate percentage of biologically false positive reactions shown in this tabulation is an average estimate of the frequency of positive serological tests for syphilis in many reported series. Individual reports vary enormously, depending on the various factors previously enumerated.

Moore & Mohr express the opinion that in certain population groups of the United States of America with a low syphilis rate at least half the seropositive reactors discovered in mass blood-testing programmes do not have syphilis at all but do instead have biologically false positive reactions.
These workers have very conveniently classified non-syphilitic reactions into two categories, acute and chronic biologically false positive reactions.

**Acute Biologically False Positive Reactions**

The acute biologically false positive reactions are those attributed to a variety of infections, bacterial, viral, plasmodial, rickettsial, or protozoal. They appear during or subsequent to such diseases and regress spontaneously to normality within a relatively short period of time, not exceeding six months.

Some years ago Levrè observed the non-specific seroreactions of patients with respiratory system diseases and added a study of 74 patients of his own with bronchitis and influenzal bronchopneumonia. Eight of these patients had positive serological reactions; four had false positive reactions due to the respiratory disease.

Wiedemann stated that non-specific positive reactions to the tests for syphilis are often found in the course of scarlet fever or convalescence therefrom. These reactions are most frequent during the second week of illness and their relative intensity is most marked during the first week. They all become negative in a reasonably short period of time. There appears to be no clear-cut relationship to the severity of the illness. Most often only one of the complement-fixation, flocculation, or precipitation reactions is positive.

Dalton discussed the biologically false positive reactions that occur in infectious mononucleosis. Some 190 instances of positive Wassermann tests or Eagle flocculation tests were reported between 1930 and 1942. The false positive reactions returned to normal within nine weeks in nearly all the reported cases. The author recommended that serological tests for syphilis be repeated over a 12-week period before antisyphilis treatment is instituted when it is reasonably certain that the reactions are falsely positive.

There has been considerable investigation of the influence of smallpox vaccination on the development of biologically false positive reactions. Perrot reported the results of testing the sera of 390 newly enlisted recruits with no abnormalities 13 and 31 days after vaccination against smallpox. A battery of six tests, using one or two antigens of different origin, was employed: Meinicke tube clarification, Kahn, Kline, Mazzini, undescribed cardiolipin slide test, and Kolmer. At 13 days, 55 sera gave some degree of positive reaction with one test or more; 44 sera gave a single positive or doubtful reaction, and 11 gave several. The three slide tests gave no reactions. At 31 days all sera were negative to all tests except the Meinicke, which, with one of the two antigens, gave 1 doubtful reaction, 2 positive reactions, and 1 strongly positive reaction. These results suggest that vaccination is an appreciable factor in the causation of false positive
reactions to syphilis, but that such false reactions are weak and of short duration.

Of 5 000 000 persons vaccinated against smallpox in New York City during April and May 1947 a random sampling was made of approximately 25 000, who returned for a reading of the vaccination reactions. Greenberg reported on the clinical findings among these 25 000 persons. The mass vaccination campaign did not produce any noticeable increase in the number of seropositive results found during routine testing in the Department of Health laboratory of some 60 000 samples monthly. In a selected group of 133 known non-syphilitics tested with four tests (Mazzini, Kahn, Kolmer, VDRL) there occurred 9% false positive serological reactions for syphilis, but there are no difficulties in distinguishing these reactions from true syphilitic reactions. The serological reactions were of low titre and became negative spontaneously within a period of three to four months. De Lavergne and his co-workers subjected the sera of 9842 Italian workmen to the Wassermann test. The reactions of 144 serum specimens (1.4%) were found to be positive. The men were later vaccinated against smallpox. Of those who were seronegative in the Wassermann test 108 became available for blood sampling some 28 days after the smallpox vaccination, and of these, 19 (17%) showed positive reactions, with 14 weakly positive and 5 strongly positive, on being tested with a battery of seven serological tests. Only 14 were available for continued observation, and of these 11 became negative within 115 days, 1 in 117 days, 1 in 129 days, and 1 in 165 days after the vaccination.

In a very instructive article discussing the relationship between biologically false positive reactions for syphilis in patients with lymphogranuloma venereum, Simpson concludes that previous reports stating the frequency of such reactions to be as high as 36% have greatly over-estimated the true percentage. He emphasized the frequent co-existence of syphilis and lymphogranuloma venereum. In his own series of 200 cases of the disease he was able to prove only 3% biologically false positive reactions for syphilis.

In a study of serological responses to experimental inoculation with vivax malaria in human volunteers, Olansky, Harris & Hill performed 5 lipoidal tests and the Treponema pallidum immobilization (TPI) test on 130 persons. Blood was drawn before inoculation and approximately 10 days after the maximum parasite counts in the blood were obtained. Tests for reagin were positive or doubtful in 3.8%-82.3% of the post-inoculation specimens. Serological tests employing cardiolipin showed a markedly lower frequency of positive reactions than did those employing lipoidal antigens. The TPI test was positive in 19.4% of the pre-inoculation specimens and in only 9.7% of the post-inoculation specimens. In only two cases was the TPI test reactive in the same patients both before and after inoculation. Since all these volunteers were screened for absence of
syphilitic infection, it would appear that some technical difficulties in the
laboratory interfered with the accurate performance of the TPI test.

According to Kail & Marcus\(^{10}\) the injection of heterologous serum can
be followed by a positive, non-syphilitic reaction even when no anaphylactic
manifestations occur. These workers observed the serological reactions of
141 ambulatory patients given tetanus antitoxin of equine origin after
injuries. Only 22 patients were observed regularly at five-day intervals.
In these patients the positive reaction (Wassermann, Meinicke, or Kahn)
appeared between the 4th and 14th day and ranged from ± to ++. The
stronger positive reactions occurred when heterologous sera had been
previously administered. Weak reactions disappeared in 2-3 weeks; stronger
(qualitative) reactions persisted over 6-17 weeks.

Gross\(^5\) reports that after prolonged ether anaesthesia the sera of non-
syphilitic persons may give temporary false positive reactions to serological
tests for syphilis. He also observed the effect of alcohol, both in vitro and
in vivo, but in no case did he observe a biologically false positive reaction.
Indeed, the author suggests that the serological reactions of patients with
small quantities of circulating reagin may temporarily become negative
following the consumption of alcohol.

It is interesting to observe that biologically false positive reactions to
serological tests for syphilis are not limited to adults. Infants who are
seronegative at birth may develop positive reactions to such tests in the
absence of syphilitic infection. Aron et al.\(^1\) classified 17 infants and children
under 2 years of age as biologically false positive reactors. Repeated clinical
examinations and X-ray films of the long bones revealed no evidence of
syphilitic infection. Positive reactions were of low titre, showed no tendency
to rise when repeated, and declined spontaneously to seronegativity without
specific antisyphilis treatment. The causative factor of the biologically
false positive reactions was found, for 7 of the children, to be immuniza-
tion—pertussis immunization, 3; diphtheria, 2; diphtheria and tetanus
combined, 1; and triple immunization, 1. In addition smallpox vaccination
accounted for 3, chickenpox for 1, upper respiratory infection for 2, and
impetigo for 1. No cause could be elicited for the remaining 3 patients.
The average duration of time from the first known positive reaction to the
serological test for syphilis to the first known negative reaction for 14 patients
in this group was less than 2 months, ranging from 2 weeks to 4 months.
The biologically false positive response in the youngest child in this group
was observed following the fifth month of life.

**Chronic Biologically False Positive Reactions**

Chronic biologically false positive reactions are those positive results
in serological tests for syphilis in non-treponemetic individuals which
persist for a period of years, or perhaps a lifetime. They are not associated
with such precipitating causes as are seen in the acute biologically false positive reactions. We shall discuss this subject particularly with respect to the implications of this phenomenon as an indicator of possible significant systemic disease which would otherwise go unrecognized.

It should be emphasized that certain rigid criteria must be observed in order to exclude syphilis in this group of reactors. These individuals should have no anamnestic or clinical evidence of syphilitic disease. Examination of the cardiovascular and central nervous systems, including a study of the spinal fluid, must be negative with respect to syphilis. Finally, and perhaps most important, the sera of these individuals should give negative reactions with the newer specific tests developed by Nelson and his co-workers,\textsuperscript{19, 20} i.e., the \textit{Treponema pallidum} immobilization (TPI) test, and the \textit{Treponema pallidum} immune adherence (TPIA) test. These procedures depend upon the existence of specific treponemal antibodies which are separate and distinct from the non-specific antilipoidal or reagin antibodies found in routine serological tests for syphilis.

Increasing evidence is accumulating to the effect that individuals with chronic biologically false positive tests for syphilis should not be dismissed from observation merely because syphilis has been ruled out. In a very significant study Moore \& Mohr \textsuperscript{17} subjected 51 such reactors to detailed anamnestic, physical, and laboratory examinations, including haemogram, urine studies, total serum protein, albumin-globulin ratio, cephalin-flocculation and thymol-turbidity tests, search for lupus erythematosus cells in the peripheral blood, etc. Of these all but six reactors showed some significant abnormality, other than the biologically false positive reaction. Five patients had proved "collagen" diseases (disseminated lupus erythematosus in four, rheumatoid arthritis in one). One patient each had sarcoid, Hodgkin's disease, and Gaucher's disease. In 21 others there was a history or physical evidence suggesting one of the collagen diseases (disseminated lupus erythematosus, rheumatoid arthritis, periarteritis nodosa, or rheumatic fever). Two others were suspected of having sarcoid. All these 23 "suspects", and 14 other patients who were clinically normal, showed some laboratory abnormalities other than the biologically false positive reaction. The most common of these were elevation of the erythrocyte sedimentation rate and abnormal cephalin-flocculation and thymol-turbidity tests. These laboratory abnormalities are those commonly associated with clinical evidence of collagen disease.

Rein \& Kostant \textsuperscript{26} demonstrated the frequency of biologically false positive reactions in all varieties of lupus erythematosus, including the chronic localized discoid type. They found an aggregate frequency of 35\% in the examination of 178 sera of patients with these diseases, employing a battery of six serological tests for syphilis. The most sensitive (non-specific) tests in this study were the Kline-exclusion and Mazzini slide flocculation procedures; the least sensitive were the VDRL and Rein-Bossak cardiolipin
slide flocculation tests. These workers recognized, moreover, that such
serological phenomena may be the first and only sign of lupus erythematous
and may warn of impending clinical activity. Haserick & Long 6 enlarged
upon this observation and reported five cases where biologically false
positive reactions antedated by one to seven years the onset of clinical
manifestations of lupus erythematous. They concluded that patients with
positive serological tests for syphilis and atypical rheumatoid arthritis,
rheumatic fever, or glomerulonephritis may actually have latent systemic
lupus erythematous. They recommended the plasma lupus erythematous
test as a diagnostic procedure in such cases. Miller and his co-workers 15
likewise investigated a group of 14 patients with biologically false positive
reactions whom they considered might later suffer from systemic disease.
These patients had one or more of the following signs or symptoms: polyarthritis, vague pains, transient rashes, splenomegaly, epilepsy, anaemia, abortions, headache, scotoma, and weakness of the extremities.

In addition to the group of diseases discussed above, the most important
condition associated with chronic biologically false positive reactions is
leprosy. Moore & Mohr 17 state the incidence of such reactions to be
variously reported as from 40% to 60%. An excellent survey of this
problem in India was accomplished by Kvittingen and his group. 11 They
examined 955 serum samples at the WHO Venereal Disease Demonstration
Team’s Laboratory at Simla. Their results varied from 3.2% positive in a
group of 253 leprosy sera from Ceylon, using a slide modification of the
Meinicke test, to 80.7% positive in a group of sera from the Sabathu
Leper Home in India, examined with the Kahn test. While no attempt
was made to rule out syphilis with the specific tests of Nelson, in a special
group of sera from 25 lepers with no anamnestic or clinical evidence of
syphilis, doubtful to positive reactions varied from 12% to 88%. All but
one of these cases were of the lepromatous type. In Guatemala, Portnoy,
Galvez & Cutler 85 subjected 51 leprosy patients to a battery of five sero-
logical tests for syphilis. They found a much higher percentage of
biologically false positive reactions in patients with the cutaneous form of
leprosy than in those with the neural or "podalic" forms. Varying with
the sensitivity of the test, positive or doubtful reactions were found in 35%
(Kolmer regular test) to 90% (Kahn standard test) of patients with the
cutaneous form of leprosy, and in 22% (Kolmer regular test) to 59%
(Mazzini test) of all leprosy patients. Other tests used were the VDRL
slide test and the Kolmer cardiolipin test.

Verification Tests

For many years attempts have been made by serologists to differentiate
chemically and immunologically the reactive substance in syphilitic serum
from that of non-syphilitic conditions. For this purpose numerous " verifica-
tion procedures” have been devised, including those of Hecht, Wasser- 
mann, Witebsky, and Kahn. None of these methods has been able
to distinguish consistently between true positive and false positive serological
reactions. In more recent years, Neurath and his associates have attempted
the differentiation of the two varieties of reagin antibody by means of the
euglobulin-inhibition test. These workers isolated a thermostable inhibitor
substance, which, they claim, selectively inhibits the flocculation of lipoidal
antigens by the euglobulin fraction of biologically false positive serum.
In syphilitic serum no such inhibition was noticed. On the basis of a large-
scale study of the Neurath euglobulin-inhibition phenomenon in the sero-
diagnosis of syphilis, Falcone and her associates conclude that the Neurath
procedure added no significant information to that given by the standard
serological tests for syphilis. They noted a disturbing lack of reproducibility
in the test results on repeat specimens from the same person as well as
variability when different antigens were employed.

In the course of the past eight years C. R. Rein and the present writer
have studied the Neurath procedure in approximately 5000 sera in the
laboratories of the Department of Dermatology and Syphilology at the
New York University Post-Graduate Medical School. While recognizing
certain limitations in this non-specific verification procedure, we cannot
agree with Falcone and her associates that no significant information is
added by the Neurath test. When a biological-type (BT) reaction is obtained
syphilis can be excluded in practically 100% of the cases. On the other
hand as many as 20% of non-syphilitic sera may give a syphilitic-type (ST)
Neurath reaction. We consider the Neurath test to be the most accurate
verification procedure of those based on non-specific lipoidal antigens.
The advent of the newer specific immobilization procedures of
Nelson and his co-workers has, of course, rendered obsolete all previous
attempts at verification employing non-specific lipoidal antigens.

The reliability of the Treponema pallidum immobilization (TPI) test in
differentiating between syphilis and biologically false positive reactions
has been reported by Nelson and associates, Mohr and others, Moore
& Mohr, Miller and colleagues, and Magnuson & Thompson. The
advantages of a test procedure employing dead treponemes make the more
recent Treponema pallidum immune adherence (TPIA) test more practical
in use than the TPI test. Since the details and evaluation of these procedures
are covered elsewhere in this Bulletin, suffice it to say that these phenomena
based on specific treponemal antigen-antibody reactions offer the most
accurate means of differentiating between true and false positive serological
tests for syphilis.
Management of Possible Biologically False Positive Reactors

Individuals who present positive serological tests for syphilis in the absence of anamnestic or clinical evidence of the disease, including negative cardiovascular, neurological, and spinal fluid studies, should be investigated to establish the diagnosis of latent syphilis, as against biologically false positive reactions, in the following manner:

1. Repeated quantitative serological tests should be performed. In the case of acute biologically false positive reactions serological titres are usually low and tend to decline to seronegativity over a period of two to six months. Therapy should be withheld for this time to afford the patient the opportunity of reverting to spontaneous seronegativity. The chronic biologically false positive reactor may show higher titres, but these usually show no tendency to rise or fall.

2. A battery of serological tests employing crude lipoidal antigens and cardiolipin antigens should be performed. Serological patterns obtained with such a battery (e.g., Mazzini against VDRL; Kline exclusion against Rein-Bossak) often suggest a syphilitic reaction or a biologically false positive reaction. Where positive reactions are obtained with the crude lipoidal antigens and negative ones with the antigens employing cardiolipin, one is almost invariably dealing with a biologically false positive reaction. Where similar or higher titres are present in serological reactions with the cardiolipin antigens, the likelihood of a true syphilitic reaction is greater.

3. An attempt should be made to discover those diseases capable of producing biologically false positive reactions. This is particularly important in the case of the chronic biologically false positive reactor. In these cases a thorough investigation should be made to rule out systemic disease, especially collagen disturbances. Investigation should include serum protein studies, erythrocyte sedimentation rate, search for the lupus erythematosus cell, liver function studies, urine studies, and haemogram.

4. Where the aforementioned investigative procedures are inconclusive, the ultimate test procedure should be the TPI or TPIA test. These two procedures devised by Nelson and his co-workers offer the best available means of differentiating between true syphilitic and biologically false positive reactions.

5. Where adequate facilities are not available or there is poor cooperation from the patient, therapy should be administered to prevent the possible development of late syphilitic sequelae.

6. Once therapy is administered, the patient should be considered a probable latent syphilitic and should be afforded the same follow-up as a treated proved latent syphilitic.

7. The chronic biologically false positive reactor may be correctly identified even after, and in spite of, antisyphilis treatment.
RÉSUMÉ

La réactivité des sérum d'individus non atteints de treponématoses avec les antigènes lipoidiques ou cardiolipidiques, c'est-à-dire la production de fausses réactions positives lors des épreuves sérologiques, retient de plus en plus l'attention. La fréquence de ces réactions semble actuellement s'accroître, alors que les réactions syphilitiques vraies deviennent plus rares à la suite du traitement généralisé par les antibiotiques. En outre, la mise au point des tests treponémiques, tels que le TPI et le TPIA, qui permettent dans une certaine mesure de distinguer les vraies réactions des fausses a donné à ce problème un regain d'actualité.

Le mécanisme des fausses réactions n'est pas mieux connu que celui des vraies et les recherches biochimiques n'ont pas confirmé les nombreuses hypothèses avancées pour les expliquer.

La fréquence des réactions faussement positives dépend de divers facteurs, tels que la stabilité immunologique du sujet — aisément troublée chez certains individus par la présence d'une infection — et le type de test utilisé — moins l'antigène lipoidique est pur, plus sont grands les risques de fausses réactions.

Un certain nombre de maladies peuvent être à l'origine de fausses réactions positives. Moore et Mohr en ont dressé une liste et ont indiqué la proportion approximative de fausses réactions qu'elles pouvaient causer. Ils ont classé ces réactions en aiguës et chroniques.

Les fausses réactions positives aiguës ont pour origine des infections bactériennes, virales, rickettiennes ou parasitaires (maladies de l'appareil respiratoire, mononucléose infectieuse, vaccinations diverses des enfants, paludisme) ou l'injection de sérum hétérologue, l'effet de l'alcool, l'anesthésie à l'éther, par exemple. Elles apparaissent et disparaissent avec l'état pathologique qui les a provoquées, ou peu après.

Les réactions chroniques, au contraire, s'observent durant des années, parfois toute la vie. Elles peuvent avoir pour origine un état pathologique général passé inaperçu et sont parfois l'indice de maladies du collagène. On a même signalé des réactions faussement positives qui ont précédé de 1 à 7 ans l'apparition de symptômes de lupus erythematous.

L'infection qui engendre le plus de réactions faussement positives est la lèpre. La proportion des fausses réactions chez les sujets atteints de lèpre diffère selon le test employé. On a signalé des proportions variant entre 3% environ, avec la modification sur lame du test de Meinicke, et 80% environ avec le test de Kahn.

L'auteur indique quelles sont les épreuves sérologiques et les recherches diagnostiques à effectuer afin de distinguer les réactions faussement positives de celles qui indiquent une syphilis latente. En dernière analyse, on recourra aux tests TPI et TPIA qui représentent actuellement les meilleurs critères de différenciation.

REFERENCES

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