

FOLLOW UP OF TREATMENT OF NEUROSYPHILIS

By

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INTRODUCTION

The title of this paper appears to be clear cut but as we shall presently see requires to be modified in many ways and should convey some suggestion of the difficulties encountered in an analysis of this nature.

Penicillin is a valuable adjunct to the treatment of syphilis and undoubtedly remains as the most important therapeutic measure. However there has been some difference of opinion regarding the value and desirability of its exclusive use, in cases of syphilis of the CNS. In this paper it is not the intention to consider the aspects under the many diagnostic entities of neurosyphilis, but to emphasise certain general features and present a broad outline summary of the experience with penicillin and Bismuth therapy in the treatment, particularly in the neuroaxis involvement and the progress in the follow up of a group of such cases in the post treatment observation period.

Basic Considerations. For accurate follow up and evaluation of therapy in neurosyphilis a knowledge is required on several basic points. First, we must know something about the outcome of the untreated disease and its natural course in order to evaluate and compare the success or failure of the particular therapy used. Second, we must have a knowledge of the characteristic ability of the preparation used to maintain a continuous treponemicidal blood duration level and methods to estimate on a laboratory basis the action of therapy of the various time dose relationships of the drug used.

Third, a correct study of the spinal fluid syndromes at the varying phases of neuroaxis involvement and the characteristic changes in the CSF pattern and their significance to forecast the prognostic outcome in each case.

Fourth, a most concise descriptive terminology which is desirable to differentiate between the CSF which indicate syphilitic activity or inactivity, healing or arrest of the pathological process in the cerebro-spinal axis.

Fifth, a reliable criterion of therapeutic efficacy or failure in a given case capable of accurate interpretation to determine and estimate the progression or regression in relation to adequate treatment.

To compare the degree of success or failure of the therapy a knowledge of these basic points is essential to allow epidemiological and statistical evaluation with the present day methods. Also the results of treatment are affected by many still unsolved problems. The preventive effect of treatment of early syphilis in the incidence of eventual neuro-axis involvement and the influence of the epidemiological factors on the outcome remains illdefined.

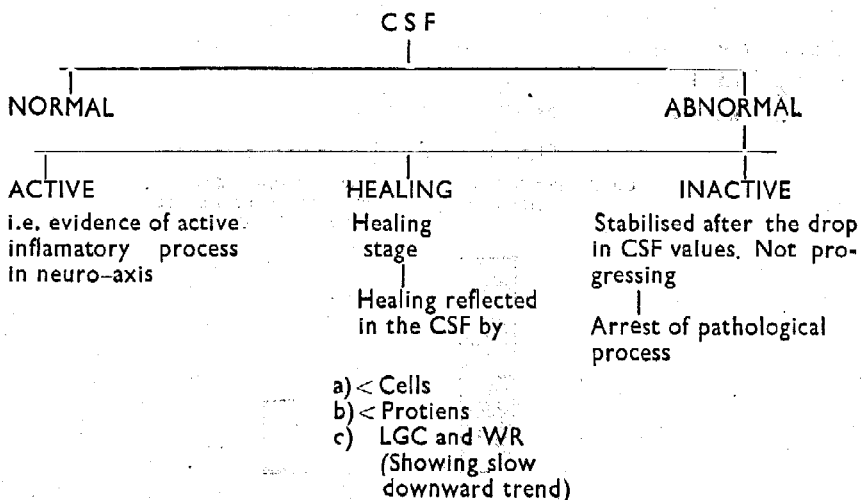
It is beyond the scope of this paper to discuss all the basic considerations. However brief comments on few of the points are of particular interest. Present scientific methods demand evaluation of the effectiveness of new drugs, only on the basis of comparative data collected from treated patients and untreated infected control group.

A retrospective analysis of the ultimate fate of untreated syphilitics as revealed by BOECK-BRUUSS-GARRD JESTLAND material indicate that of 887 untreated patients followed for 30 years, neurosyphilis occurred in 6.5% and the neuro-axis involvement was almost twice as frequent in males as compared to females (9.2 versus 5.1%).

The importance of these findings in evaluating the results of modern methods of therapy is evident but the possibility cannot be excluded that the disease to a certain extent has undergone changes in its character since the turn of the century, with alterations in the biology of syphilitic involvement of the CNS not only by modern rapid intensive treatment for early syphilis but by penicillin therapy incidentally given for many un-related conditions.

The time dose schedules, the preparations to be used and the need for certain criteria for long acting penicillin, have been emphasized and established by the WHO.

Terminology: Is very important that more uniform terminology be adopted to describe the CSF findings of patients with CNS syphilis. The terms, standard, typical etc. are vague and subject to misinterpretation. The best and the most concise descriptive term to differentiate between CSF which indicate syphilitic activity would be what is known as Dattner-Thomas Spinal Fluid Formula which gives an indication of the extent and severity of the neuro-axis involvement, serve as a reckonable criterion for evaluation of treatment and also enables one to make an opinion of the prognostic outcome of the case.



PRECISE CRITERION OF THERAPEUTIC EFFICACY OR FAILURE

This will be referred to in the subsequent part of the paper,

Material and Methods: In this report the results of treatment and progress with penicillin and bismuth in two separate groups of cases of late neurosyphilis are presented.

A. *Clinical:* The first group dealing with the critical pattern study on the clinical assessment of 51 cases of neurosyphilis inclusive of many diagnostic categories (period between 1950-59).

B. *CSF Syndrom:-Serial Study:* The second group is from the analysis of the serial examination in 250 cases of late syphilis which showed CSF abnormalities indicative of definite neuro-axis involvement.

Selection of Cases: In both the groups the patients have been selected on the following basis:

1. Only patients who received the following schedule doses of penicillin and bismuth are included.

Penicillin—9.8 MU Total.

Bismuth—0.2 Grams IM weekly of 10 each 3 such courses with an interval of 4 weeks between each course.

Bismuth and Iodides: All symptomatic cases were given Pot Iodide orally and bismuth IM for 2 or 3 weeks prior to starting of penicillan therapy, unless penicillin was specially warranted from the beginning itself.

CLINICAL ASSESSMENT -FOLLOW UP-FIRST GROUP

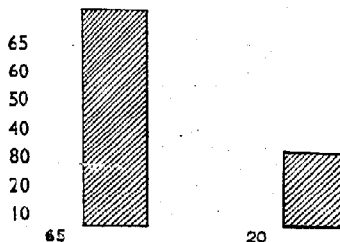
The important subjective symptoms and the objective signs from the 51 cases of neurosyphilis examined have been elicited, analytically recorded and grouped for a pattern study of the neuro-axis involvement and the frequency of the findings have been totalled up. Co-existence of multiple number of findings in the same patient have been recorded and accounted for.

Subsequent physical examination after therapy during the surveillance period from 120-180 & 180-270 "Zone days period" was systematically done and the clinical findings again analytically recorded and the progress and frequency of the findings totalled up.

The findings are diagrammatically represented.

FREQUENCY OF FINDINGS

Subjective Symptoms Before therapy	Group Pattern Study After therapy Surveillance period 120-180 days
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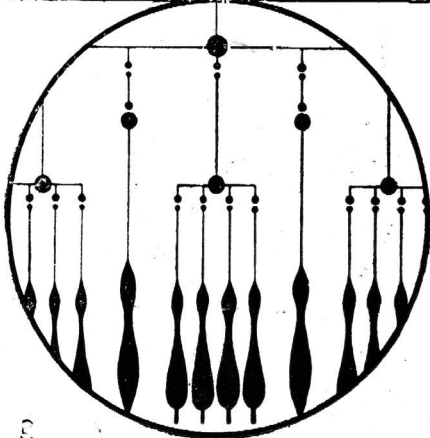


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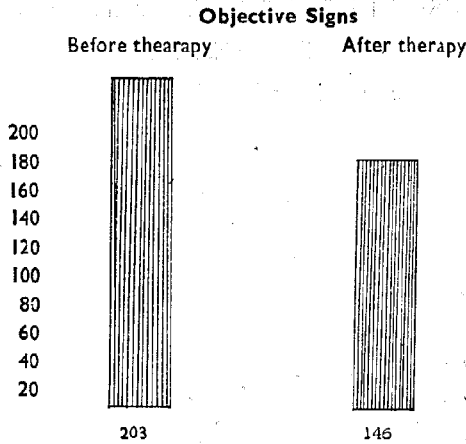
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Vitamin C B.P.	

INDICATIONS:

- Fevers
- Infections
- Hypermetabolism
- Pregnancy
- Lactation
- Restricted diet
- Peptic ulcer
- Gastro-intestinal disorders
- Diabetes
- Neuritis, etc.



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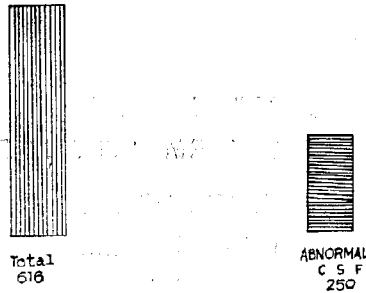


CSF SYNDROME SERIAL STUDY SECOND GROUP

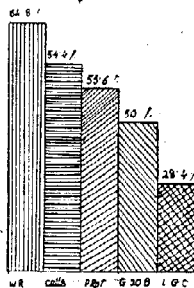
The 2nd aspect of the study is from the case material for the period from 1947-1955.

The case material is sufficiently large representative of all diagnostic categories of neurosyphilis and statistically significant for evaluation of progress. The graphs and diagrams that follow deal with the criterion of therapeutic efficacy or failure, the prognostic interpretation of the serial examination of CSF in all types of neurosyphilis, the response to the therapy and the progress as reflected in the CSF.

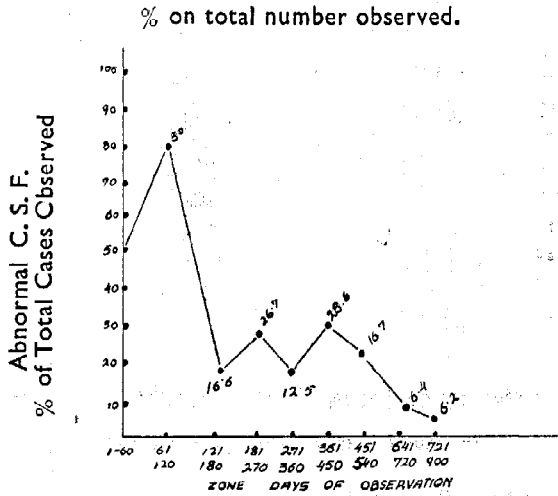
A full analysis of the CSF in 616 cases prior to treatment yielded the following abnormal findings.



Analysis of type of CSF abnormalities in 250 cases at pretreatment phase:—



ANALYSIS OF PROGRESS IN TERMS OF ATTAINMENT/MAINTENANCE OF CSF NORMALITY



Here association of different types of abnormalities on the same patient have not been shown separately.

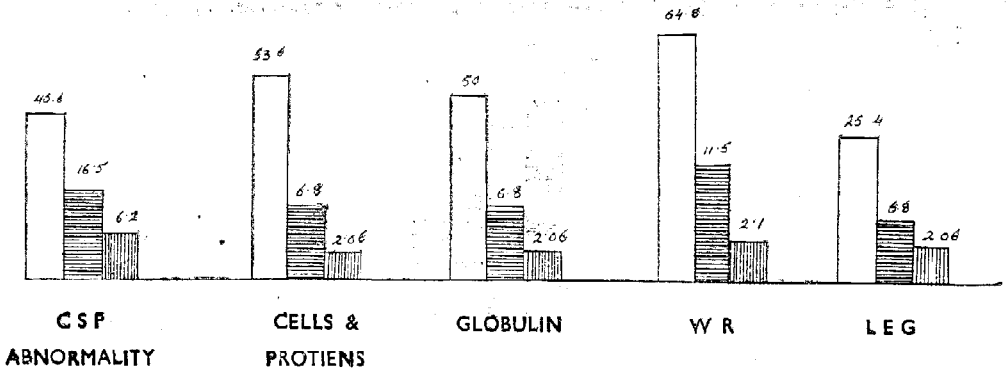
From the findings as represented in the graph only 16.5% showed abnormality by the 3rd zone going down to 6.2% by the 9th zone of observation period,

ANALYSIS OF PROGRESS IN TERMS OF BEHAVIOUR IN TYPE ABNORMALITY CSF %

PRETREATMENT.....P

Zone days 180Z3

“ “ 900Z9



DISCUSSION

Progress follow up study

Clinical Evaluation Follow Up

From the above findings it is apparent that in spite of adequate therapy the objective findings show no demonstrable, significant reckonable changes after the therapy. The frequency of findings especially the objective signs remain as high as 146 as compared to 203 in the pre-treatment stage.

In the subjective symptoms the frequency of findings is 20 compared to 65 in the pretreatment stage.

In late syphilis with involvement of the CNS as a result of treatment; the arrest, resolution or transformation of syphilitic process cannot guarantee the restoration of function and replacement of anatomical structures damaged although TP destruction may be ensured.

Thus in the symptomatic analysis we are partly dependent on the subjective statements of the patient which are at best vague and in exact, or on the objective signs which in many cases remain unchanged in spite of successful treatment as indicated above.

Again improvement or deterioration is difficult to infer in cases of CNS syphilis because physicians vary in their probe and elucidation of clinical phenomena involved, the reaction to the disease is different in each case and often in the same patient from time to time.

So evaluation of therapy and progress purely on clinical grounds have very great limitations. Unless a series of individual case protocols are presented displaying over a period of years the various types of response to indicate success or failure in the progress of individual cases.

Hence criterion of therapeutic efficacy and progress in a group pattern study on clinical grounds is considered to be unreliable and not capable of accurate interpretation for assessment of results of therapy.

CSF SYNDROME STUDY EVALUATION 2nd GROUP

Changes in the abnormal CSF following treatment offer a more reliable criterion of therapeutic efficacy or failure than clinical signs and symptoms.

It is well known that even the most severe forms of neurosyphilis (GPI) if untreated has a constant characteristic spinal fluid syndrome. This is true of all types of neurosyphilis as evidenced by high proportion of patients showing improvement in the CSF abnormalities regardless whether they are treated for asymptomatic neurosyphilis or GPI.

This must conspicuously be so because in all types of neurosyphilis the response to therapy as reflected in the CSF findings is the direct result of the effect of treat-

ment on TP and not upon the structural changes and the subsequent resulting clinical manifestations.

Also after quantitative values of great accuracy became available for the cytological, biochemical and colloidal gold tests it became even more apparent that if there is an arrest or increase in the activity of the inflammatory or degenerative process indicating on one hand success and on the other hand failure of therapy, there is always a corresponding decrease or increase in the numerical values of the CSF test.

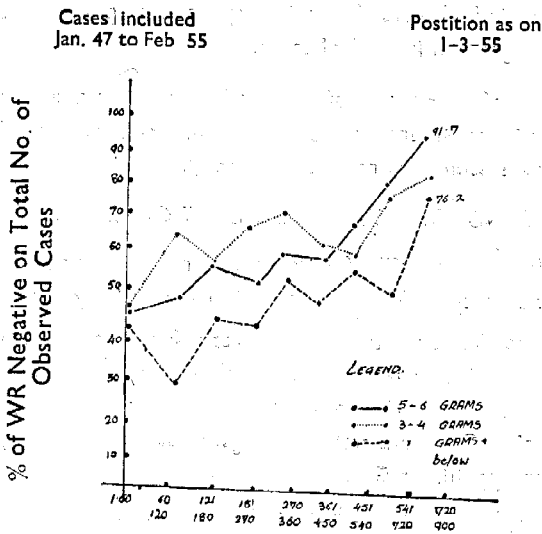
And in the asymptomatic group there is no other alternative to determine the progression or regression.

Because of this CSF fluid abnormalities comprise the most substantive basis as a precise and definite indicator to estimate and determine the progression or regression in a case after adequate therapy and capable of accurate interpretation to evaluate upto the extreme degree. CSF is the mirror in which the infection is reflected and serial examinations give an impressive account of what the therapy has actually accomplished and the progress measured by spinal fluid examination.

Hence in the second group of patients the progress and follow up interpretation is based almost entirely on the result of repeated examination and the spinal fluid alone used as sole index of comparison.

The CSF values in all types of neurosyphilis cases in the pre and post treatment phase at varying periods of surveillance in "Zone days" upto 900 days have been recorded. 83.5% became normal by the 3rd zone going up to 93.6% by the 9th.

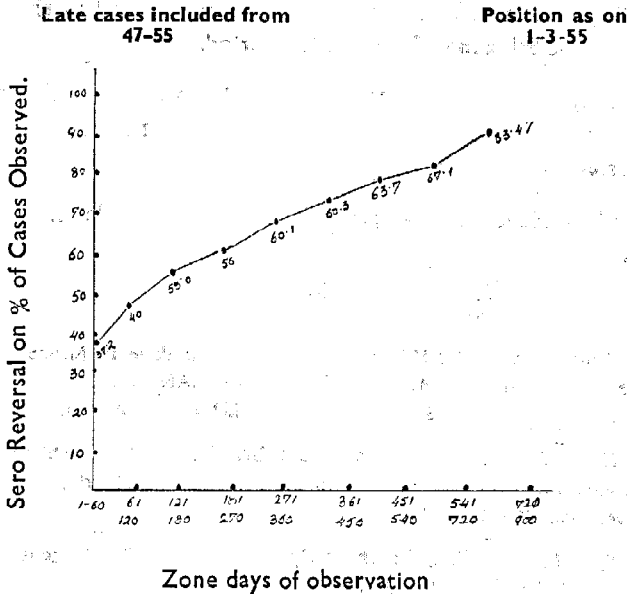
ANALYSIS OF PROGRESS IN TERMS OF BISMUTH TOTAL QUANTITY VARYING FROM 1 GRAM AND BELOW TO 6 GRAMS AT POST TREATMENT PHASE.



This became possible since some cases did not complete the Bismuth therapy. From comparison of cases which received 1 Gram and below with those that received 5-6 Grams it is evident that better sero-reversal has been achieved with higher Bismuth therapy.

The sero-reversal in the 9th zone is 76.2% as compared to 91.7% for higher Bismuth group in this unselected series.

Analysis of progress in terms of SEROLOGY SEROLOGICAL STATUS DETERMINED BY W R.



Sero Reversal: Highly satisfactory outcome In the first zone sero reversal was achieved in 37.2% and during the 9th zone 83.4%.

SUMMARY AND CONCLUSION

1. Observation during the period of surveillance of the effects of penicillin and bismuth therapy in late syphilis with neuro-axis involvement and critical study and analysis of two groups of cases of neuro-axis involvement have been presented.
2. Interpretation of progress in treatment and therapeutic efficacy have been made by (a) clinical analysis in the pre and post treatment phase in the first group of 51 cases and by (b) a CSF syndrome study in 250 cases of neuro-axis involvement by a serial examination of the CSF from the pretreatment period to and during the post treatment phase at varying periods of 'Zone level days', upto 900 days in many cases.
3. The limitations in judging the therapeutic efficacy and progress in treatment solely by clinical evaluation in neurosyphilis and the importance of CSF serial

study forming the most substantive basis as a precise and definite indicator to estimate and determine the progress of treatment and capable of accurate interpretation to evaluate upto the extreme degree has been brought out.

4. Treatment schedule was 9.6 MU of penicillin and 3 courses of bismuth of 10 injection of 0.2 Grams each. Total of 6 Grams and the findings represent the results achieved from a combined therapy schedule.

5. Treatment results in terms of improvement in clinical manifestations and of achievement of CSF normality have been indicated as diagramatic and graphic representations. In the CSF findings 83.5% became normal by the 3rd zone going up to 93.6% by the 9th zone of observation period.

6. The importance of bismuth in combination with penicillin in treatment of late syphilis has been brought out although no comparative control study without has been carried out.

7. Results achieved from a combined therapy schedule appear to be highly satisfactory.

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