2. Emphasis is placed on the fact that osteoporosis is not a disorder of calcium metabolism but rather an atrophy of the bone matrix.

3. Factors in the causation of osteoporosis are disuse and senescence; that faulty diet is a factor, in our opinion, has not been established.

4. Because of the constant tendency of osteoporosis to occur in women after the menopause and the beneficial effect of estrogen therapy on the retention of calcium in this condition, we believe that the postmenopausal state is the most common etiologic factor.

5. Of 42 patients under the age of 65 with generalized osteoporosis, 40 were women who had gone through the menopause (physiologic 30 cases, artificial 10 cases); only 2 were men; there were no cases in women before the menopause.

6. Three of the 42 patients had had thyrotoxicosis; whether this had been a factor in the causation of the disease it is impossible to state.

7. Postmenopausal osteoporosis has a predilection to involve the spine and the pelvis; the long bones are less likely to be involved; the skull, in contrast to osteitis fibrosa generalisata, is almost never involved.

8. There is considerable evidence that patients with postmenopausal osteoporosis have a tendency to atrophy of other tissues, notably the skin.

9. In 2 cases postmenopausal osteoporosis was complicated by superimposed Paget's disease; the modification of the latter disease by the former is noteworthy.

10. One case of postmenopausal osteoporosis was complicated by superimposed hyperparathyroidism; the latter disease was modified by the former.

TREATMENT OF DEMENTIA PARALYTICA

A FIVE YEAR COMPARATIVE STUDY OF ARTIFICIAL FEVER THERAPY AND THERAPEUTIC MALARIA IN TWO HUNDRED AND THIRTY-TWO CASES

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AND
FRANKLIN G. EBAUGH, M.D.
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This is a report of a five year study comparing the therapeutic efficiency of artificial fever therapy and of therapeutic malaria. The preliminary report of this study was made in 1936. There is nothing unique in the use of either malarial therapy or artificial fever, the former having been advocated by Wagner von Jauregg's original report in 1917 and the latter by Neymann and Osborne in 1929. For reasons not entirely clear to us certain clinics treating patients with neurosyphilis have been skeptical of the therapeutic value of artificial fever in this neuropsychiatric disorder. Because of this apparent prejudice against a new method we felt it wise to observe a series of patients, taking alternate patients in the series for treatment with each method. Patients were assigned to the artificial fever or malaria series in alternation as they were admitted to the Colorado Psychopathic Hospital and Clinic, that is, patient 1 went to the malaria series, patient 2 to the artificial fever series and so on. The postfever care has been according to the same plan in all cases from both series and has consisted of intensive chemotherapy to trypanosomal, nearosamine and bismuth compounds according to the plan given in the accompanying outline.

Since the inauguration of this study there have been numerous reports advocating the use of artificial fever therapy in the treatment of neurosyphilis and others reporting on the present status of therapeutic malaria. The best statistical analysis of a comparison of the therapeutic efficiency of the two methods used independently has been made by the Cooperative Clinic Group. The historical background of this study was traced in the preliminary report and will not be repeated here.

METHOD

All patients treated by both methods were subjected to detailed clinical and laboratory studies before treatment was instituted. All were studied by one of us. The treatment of all patients in both the malaria and artificial fever series was administered in the clinic under our direct observation and supervision. Follow-up studies were made at six month intervals in the outpatient department of the Colorado Psychopathic Hospital except when the patients were incarcerated in the Colorado State Hospital. In such cases the follow-up studies were made by a physician from the Colorado Psychopathic Hospital. The majority of the postfever chemotherapy was administered in the outpatient department of the Colorado Psychopathic Hospital, although a few patients received their treatment from private physicians according to our therapeutic plan. Because of the cooperation of these private physicians and the staff of the Colorado State Hospital there is little difference in the type of follow-up care of these patients treated outside the Colorado Psychopathic Hospital Clinic. Social data, appointments for follow-up examinations and general aid in keeping track of the patients were handled efficiently by a trained psychiatric social worker who has this study as her principal duty. All follow-up examinations were made by a trained psychiatrist on duty in the hospital or in the Colorado State Hospital. The physicians making these follow-up studies were not aware of which type of fever therapy the patient had originally received. The patients in the malaria series in most instances received fifty hours of fever at 104 F. or more, although at times the patient's condition would not allow this amount of fever to be given. In the first three years of the study patients in the artificial fever series received fifty hours of fever at rectal temperatures of 105 F. to 106 F., given as ten treatments of five hours each. During the last two years of the study the artificial fever group received only thirty-six hours of fever but at a rectal tempera-

From the Colorado Psychopathic Hospital, University of Colorado School of Medicine.


ture of 105.8 F. given as twelve treatments of three hours each. We could notice no difference in the results obtained from the shorter, more frequent treatments, and it enabled us to treat a greater number of patients in the artificial fever department. After fever therapy by either method complete laboratory and clinical studies were again made. Patients responding favorably were transferred to the outpatient department and reported weekly for follow-up treatment. A small percentage returned to their private physicians for follow-up care, but they were encouraged to return to the clinic each six months for reexamination. The social worker keeps a rotating roster, and each six months each patient’s name appears automatically. She then makes contact with the patient and arranges for a reexamination in the clinic. Those patients transferred to the state hospital in Pueblo are checked in that institution. We have had the usual difficulty in following our patients in their travels about the country, but the assignment of a social service worker to the task of getting the patients in for examination has made our follow-up treatments and examinations more complete than was possible prior to the inauguration of this system. For example, we were able to follow all of our patients treated with malaria and reported in the preliminary study and 66 per cent of the artificial fever series studied in the same group for the entire five years or until they died. The periodic reexaminations consist of complete physical, neurologic and mental check-ups and serologic examinations of the blood and spinal fluid. It is interesting to note that most of the patients lost sight of during the follow-up period were patients who responded favorably to treatment and after two or three years of follow-up care felt free of symptoms and refused to come back for further examination. Some of those lost sight of moved out of the state and could not be reached. Most of the patients doing poorly have been admitted to the state hospital or have continued to come to this clinic seeking aid for their trouble. The deaths are, as far as we know, all recorded in the data.

RESULTS

The statistical evaluation of the results of any clinical research study is difficult at best. In a disease such as neurosyphilis there are so many variables, such as the duration of the infection before treatment, the type and quantity of prefever chemotherapy, the age and the physical and social status of the patient, that any statistical presentation is open to criticism. A detailed statistical analysis of a large group of cases was made by the Cooperative Clinical Group. We supplied a number of the cases in that study, and both the fever and the malaria series of the first year were included in that survey. We do not feel competent to make a detailed statistical breakdown of our data. We wish to present our general results and to mention certain trends noted in individual cases.

That the series are fairly comparable is indicated by the fact that 32 per cent of the patients in the artificial fever series and 31 per cent of those in the therapeutic malaria series were persons with advanced or so-called group A dementia paralytica. The average age of the artificial fever group was 40 years, and the average of the malaria group was 42.6 years, and the duration of symptoms prior to treatment was twenty-two and four-fifths months in the fever group and seventeen and one-fifth months in the malaria group. The data concerning prefever chemotherapy included vague recollections of “shots” taken years before the development of dementia paralytica as well as accurate clinical records from other hospitals and clinics. The reliability of the data varied so greatly in both series that no attempt was made at any evaluation of the influence it may have had on the course of the disease.

It will be noted in table 1 that more patients were treated by artificial fever than by therapeutic malaria. This was not due to variation in the selection of cases, but we have included in the artificial fever group 37 patients rejected from the comparative study because of the presence of diabetes, healed tuberculosis, cerebral arteriosclerosis, chronic nephritis and mild cardiac decompensation. Patients suffering from these disorders are not suitable for malaria therapy but may be given artificial fever with caution. In some instances the rectal temperature of the artificial fever was lowered to 104 F. It was felt, however, after a study of these cases that they should be lumped with the other cases suitable for either form of treatment in that these disorders probably do not greatly influence the course of the neurosyphilis other than by contraindicating malaria therapy. The results in this small group did not significantly alter the general picture.

### Table 1—Types of Treatment and Clinical Results

<table>
<thead>
<tr>
<th>Artificial Fever</th>
<th>Therapeutic Malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimission</td>
<td>25</td>
</tr>
<tr>
<td>Improved</td>
<td>19</td>
</tr>
<tr>
<td>Unimproved</td>
<td>31</td>
</tr>
<tr>
<td>Died within three months of treatment</td>
<td>9</td>
</tr>
<tr>
<td>Died subsequently</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>134</td>
</tr>
</tbody>
</table>

The general results of the study are included in table 1. Remission or improvement was noted in 59 per cent of the artificial fever group as compared with 58 per cent in the therapeutic malaria group. By remission is meant the condition of patients who are showing no clinical symptoms of their disorder and who have been able to resume their previous role in the community. Improved patients are those who are definitely better than when treatment was instituted but are operating at a lowered level of efficiency. The inter-
esting fact is that there was approximately the same
difference between the two series in the preliminary
or first year of this study. In other words, the rate of
improvement during follow-up care and the rate of
relapse are approximately the same in the two series,
and the difference in our hands seems to be a difference
in immediate results.

Table 2.—Group Classification in Relation to Clinical Results

<table>
<thead>
<tr>
<th>Artificial Fever</th>
<th>Therapeutic Malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
</tr>
<tr>
<td></td>
<td>No. %</td>
</tr>
<tr>
<td>Resolved</td>
<td>0</td>
</tr>
<tr>
<td>Improved</td>
<td>18</td>
</tr>
<tr>
<td>Unimproved</td>
<td>4</td>
</tr>
<tr>
<td>Died</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
</tr>
</tbody>
</table>

We cannot be certain as to the reasons for this
difference, but some of the factors which may play a
role will be mentioned. The most important differ-
ence in the two series may be the fact that with
artificial fever therapy the patients may be safely treated
at higher levels of temperature than is possible with
therapeutic malaria. The importance of high levels of
temperature has been shown by the Cooperative Clinical
Group study. Another factor which may play a role
is that patients usually gain weight during artificial
fever therapy and in most instances are in better physical
condition at the conclusion of the febrile period than
when it was first instituted. The patients with malaria,
on the other hand, usually lose weight and have some
degree of anemia in spite of energetic attempts to pre-
vent it. We originally felt that the difference was
largely due to the fact that we administered trypars-
amide with each artificial fever treatment. In order to
check on this for the last two years of this study we
did not give tryparsamide during the period of fever.
In place of this, half of the patients with artificial fever
received 0.3 Gm. of neacrophenantine and 0.26 Gm.
of bismuth salicylate during every other heating and the
other half of the patients treated with artificial fever
during the same period received no chemotherapy. We
could see no significant difference between the two
groups, nor could we see any significant difference
between them and the larger group receiving trypars-
amide with their heating. Therefore we believe that
the first two factors are the important ones, although
the added chemotherapy must be of some benefit even
though it failed to be statistically significant in this
relatively small series.

Table 2 presents the clinical results according to the
severity of the infection. Group A is advanced or severe
dementia paralytica, group B the intermediate and
group C the mild form. Detailed definitions of this
grouping are contained in the original article. The
results are good with both methods in the mild cases
and treatment becomes progressively less effective as
the severity of the process increases. We obtained no
temporary remissions in the advanced A group by any
form of treatment, but in many instances we were able
to bring about definite improvements by either method
of nonspecific treatment. The report of the Cooperative
Clinical Group showed artificial fever to be ten times
as effective as therapeutic malaria in advanced dementia
paralytica. Our study also shows a superiority of the
artificial fever method in this group (table 2) but a
superiority of only 12 per cent.

Our experience parallels that of Solomon and others
that intensive follow-up chemotherapy is essential if
optimum sustained results are to be obtained. The
variation in results reported from various clinics might
be explained on the basis of care in follow-up treat-
ment and examinations. The fact that the results in our
series are superior to those reported in some clinics and
inferior to others may well be due to this fact. We
have found that in recent years the employment of a
social worker and a greater drive to keep patients com-
ing in for treatment and check-ups have certainly
increased the beneficial results obtained in the patients
given malaria therapy as compared to those patients
treated with malaria before this study was inaugurated.
For example, in the years 1925 to 1931 we treated 219
patients with dementia paralytica with therapeutic
malaria. Of this group 45.6 per cent showed a remis-
sion or improvement. Our present malaria series
reveals that 58 per cent of the patients are in some
manner improved by the treatment, which means an
improvement of 12.4 per cent in results from therapeutic
malaria in the present study. We believe that this
difference is due largely to greater care during the
course of the malaria and greater emphasis on follow-up
chemotherapy and supervision. Both of these groups
were treated with therapeutic malaria and, incidentally,
with the same strain of tertian malaria.

The serologic response appears to show a greater
modification in the group treated with artificial fever
(table 3). The difference in results is not great and
roughly parallels the difference in the rate of clinical
remission. While we noted no direct correlation between
alteration in serologic conditions and clinical remission
in individual cases, we do find a higher percentage of
serologic reversals in the group in both series show-
ing great improvement than in those showing less
improvement or no change in clinical status. Reversal
or even great alterations in the serologic state immedi-
ately after the course of fever or malaria were rare but
when they did occur seemed to indicate a good clinical
prognosis. In several cases, on the other hand, great
clinical improvement has been maintained in persons
with spinal fluid persistently positive for syphilis.
In our small series a decrease in the cell count and protein
of the spinal fluid to within normal limits immediately
after treatment with artificial or malarial fever usually
indicated that a considerable alteration or reversal of
the Wassermann reaction and the colloidal gold curve
was to be expected in six to twelve months provided
the patient continued on the program of postfever
chemotherapy. The changes in the status of the blood
smear are inconstant and of practically no value in
evaluating either the clinical course or the status of
the spinal fluid.


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CALCIUM DEPOSITS IN THE SHOULDER AND SUBACROMIAL BURSITIS
A SURVEY OF 12,122 SHOULDERS

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The title of this paper is purposely indefinite. It is intended to cover calcium deposits observed in the tendons of the four short rotator muscles of the shoulder and the inflammatory condition of the overlying serous bursa to which these deposits do not infrequently give rise. That others have experienced difficulty in devising an appropriate label for this pathologic entity is well attested by the diversity of captions used by many who have written on the subject in the last two or three decades. It has been described as "periarticular calcifications," 1 "para-articular calcifications," 2 "subacromial" or "subdeltoid calcifications," 3 "humeroscapular" or "scapulohumeral periartitis," 4 "para-arthritis," 5 "Duplay's disease," 6 "calciated bursitis," 7 "calcite bursitis," 8 "calcification of the subacromial bursa," 9 "rheumatism" or "neuritis," 10 and "painful shoulder." 11

The fact remains that calcium deposits in the tendinous cuff which forms the capsule of the shoulder joint have for some time been recognized as a potential source of shoulder pain. The anatomy of this region, the pathologic changes encountered, the composition of the calcium deposits and their relation to the subacromial bursa are now quite well known, chiefly as the result of Codman's work on the shoulder; 12 yet little precise information is available as to the incidence of such deposits in the general population, what factors cause or contribute to their formation and what plan of treatment offers the best prospects of relief and cure of those deposits which give rise to symptoms.

Through observation of a large group of presumably normal persons over a period of years, much interesting and pertinent material on these points has been accumulated.

During the three year period from 1937 through 1939, 6,061 unselected persons were subjected to physical and fluoroscopic examination of both shoulders in connection with a routine examination at the home office of the Metropolitan Life Insurance Company; 5,061 were company employees while 1,000 were applied for insurance or for employment. Of the whole group 165 (2.7 per cent) were found to have calcium in sufficient amount to show on fluoroscopy in one or both shoulders. The incidence of calcium formation was exactly the same in the employee and the nonemployee groups.

An analysis of both groups on the basis of sex, age and occupation has been made. Since, however, it has been possible to study the 5,061 employees much more intensively and to follow them with reexamination at annual intervals, the remainder of this report will be confined to them unless expressly stated otherwise.

Before employment each applicant is subjected to a thorough physical and laboratory examination, including roentgenograms of the chest. Throughout the period of employment a detailed medical record is kept of serious and minor ailments as well as of annual physical and fluoroscopic examinations of the heart and lungs.

The 5,061 employees were taken in succession as they came for the annual health examination. They included 3,893 females and 1,178 males, of whom 89.4 per cent were under the age of 40. Seventy and nine-tenths per cent did purely or mostly clerical work, 23.2 per cent used either a typewriter or similar manually operated machine exclusively, while the remainder were employed in miscellaneous occupations such as messengers, elevator operators, porters and cleaners.

It is obvious that the group studied constitutes a selected portion of the general population as to physical condition (preemployment and annual examinations), sex (76.7 per cent females), age (89.4 per cent under 40) and occupation (94.1 per cent clerks or typists).