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

JACK R. EWALT, M.D.
AND
FRANKLIN G. EBAUGH, M.D.
DENVER

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.[1] 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[2] 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 with tryparsamide, neoarsphenamine and bismuth compounds according to the plan given in the accompanying outline.

Since the inauguration of this study there have been numerous reports[3] advocating the use of artificial fever therapy in the treatment of neurosyphilis and others reporting on the present status of therapeutic malaria.[4] 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.[5] 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 the artificial fever series was administered in this 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 this 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.

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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

Outline of Treatment of Dementia Paralytica at the Colorado Psychopathic Hospital

Therapeutic Malaria		Artificial Fever Therapy
Fifty hours at 104 F.		Thirty-six hours at 105.8 F.
Eight to ten chills	or	Twelve three hour treatments
No chemotherapy possible		Simultaneous chemotherapy

Follow-Up Treatment

A. First year:
(*a*) Six months of tryparsamide, 3 Gm. weekly
(*b*) Physical, mental, neurologic and complete serologic check-up
(*c*) Four months of bismuth salicylate, 0.26 Gm. weekly
(*d*) Two months of neoarsphenamine, 0.6 Gm. weekly
(*e*) Repeat examinations outlined under (*b*)

B. Second year:
Repeat procedure outlined for first year

C. Third year:
Repeat procedure outlined for first year

All treatment is continuous. Eyegrounds and visual fields must be checked frequently. Repeat series as often as necessary. Patients not improved after three years will probably not benefit from further treatment.

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 [1] 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.[5] 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*

	Artificial Fever		Therapeutic Malaria	
Clinical Status	No. of Cases	Percentage	No. of Cases	Percentage
Remission	25	19 } 69	7	7 } 58
Improved	68	50 }	50	51 }
Unimproved	31	22	27	27
Died within three months of treatment	2	1.4	5	5
Died subsequently	8	6.6	9	9
Total	134	99	98	99

The general results of the study are included in table 1. Remission or improvement was noted in 69 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*

	Artificial Fever						Therapeutic Malaria					
	Group A		Group B		Group C		Group A		Group B		Group C	
Clinical Status	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Remission	0	0	16	23	9	45	0	0	4	7	3	25
Improved	18	41	39	54	11	55	9	29	35	64	6	50
Unimproved	19	43	12	17	0	0	15	48	11	20	1	8
Died	7	16	3	4	0	0	7	23	5	9	2	17
Total	44	100	70	98	20	100	31	100	55	100	12	100

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 difference 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.[5] 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 prevent it. We originally felt that the difference was largely due to the fact that we administered tryparsamide 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 neoarsphenamine 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 tryparsamide 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.[1] 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 true remissions in the advanced or 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[5] 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[6] 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 treatment 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 coming 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 remission 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 in this hospital 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 showing great improvement than in those showing less improvement or no change in clinical status. Reversal or even great alterations in the serologic state immediately 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 serum are inconstant and of practically no value in evaluating either the clinical course or the status of the spinal fluid.

TABLE 3.—*Serologic Results in Cerebrospinal Fluid*

	Artificial Fever		Therapeutic Malaria	
Clinical Status	Number of Cases	Percentage	Number of Cases	Percentage
Reversed	15	11	6	6.1
Improved	47	35	28	28.5
Unmodified	47	35	40	40.8
Unable to check	25	18	24	24.4
Total	134	99	98	99.8

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CONCLUSIONS

In a five year study 232 patients with dementia paralytica have been treated with either therapeutic malaria or artificial fever therapy. The follow-up therapy in the two groups has been as nearly identical as the vagaries of clinical practice will allow. The method of therapy with artificial fever has been safer and has been productive of better results. The importance of follow-up care is emphasized. Improvement in the care of patients during malaria therapy and more attention to follow-up medication has improved the results of malaria therapy in our clinic, although these results still remain inferior to the results obtained with artificial fever therapy.

Patients with physical contraindications to therapeutic malaria may, in many instances, be safely treated with artificial fever therapy. Either method is reasonably efficient if properly managed and if general follow-up treatment and care are adequate.

The serologic responses roughly parallel the clinical results in the two series. Careful, periodic, clinical reexamination offers the best guide for therapy and gives the most reliable data for evaluation of results.

4200 East Ninth Avenue.

CALCIUM DEPOSITS IN THE SHOULDER AND SUBACROMIAL BURSITIS

A SURVEY OF 12,122 SHOULDERS

BOARDMAN MARSH BOSWORTH, M.D.

NEW YORK

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 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 periarthritis," [4] "para-arthritis," [5] "Duplay's disease," [6] "calcified bursitis," [7] "calcic 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 applicants 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 include 3,883 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).

Dr. H. H. Fellows, assistant medical director of the Metropolitan Life Insurance Company, and Drs. R. K. Felter, J. H. Inkster, Eleanor Murphy, Mary E. O'Sullivan and Peter Sabatelle assisted in this study.

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