

ARTIFICIAL FEVER

WALTER J. ZEITER, M.D.

Hyperpyrexia by physical means is definitely established as a method for treating disease. At the present time physical agents may be utilized by various methods for this procedure. These are radiant heat, luminous heat cabinets, nonluminous heat cabinets, electric blankets, high frequency electrical currents, short wave diathermy, hydrotherapeutic methods, and hot water bottle and blanket method.

I do not wish to discuss the advantages or disadvantages of any of the above methods, but rather to review briefly the results that have been obtained by the use of these methods in the treatment of various pathological conditions.

Artificial fever is not new in the armamentarium of therapeutics, various substances having been used to produce fever in patients. Among the more common, the following may be mentioned: tuberculin, sterile milk, sodium nucleinate, typhoid vaccine, suspensions of sulphur in oil, relapsing fever, sodoku, and malaria. Inoculations with typhoid vaccine and malaria are very popular. However, after the original work of Neymann and Osborne¹ in 1929 in the production of artificial fever with high frequency currents, a new field of investigation was begun and has had a very rapid development.

In a review of the literature for 1935, Krusen² found that fever produced by physical means has been recommended for the treatment of no less than fifty different diseases. Results in the treatment of the majority of these diseases have not been encouraging, although for a selected group of patients this method has given promise of great usefulness. Neymann³ has studied very thoroughly and given a comprehensive discussion of hyperpyrexia produced by physical agents. Sufficient clinical investigations have been completed in some of the following diseases so that it is safe to come to definite conclusions concerning the value of hyperpyrexia.

Gonococcic Infection: The most spectacular success has undoubtedly been obtained in the treatment of gonorrhoeal infections, including complications of prostatitis, salpingitis, periurethritis, cervicitis, and corneal ulcer. Desjardins and his coworkers⁴ state that 90 per cent of their patients with gonorrhoea, when given three to six sessions of sustained fever at 106 and 106.7° F. for five to eight hours were completely and permanently cured.

Before real effective therapy could be instituted, definite facts about the resistance of the gonococcus to heat had to be ascertained. Carpenter, Boak, Mucci and Warren⁵ determined the vitro thermal death time of 130 strains of *Neisseria gonorrhoeae* and found this to vary between 6

ARTIFICIAL FEVER

and 27 hours at 106.7° F. These findings were employed in the treatment of 11 patients with specific gonococcic infection. Each patient was subjected to a single treatment of fever at 106.7° F. which was equal in length to the thermal death time of his particular culture. There was an immediate subsidence of all clinical symptoms and a bacteriologic "cure." These same authors have treated 118 patients in addition to the 11 listed above, 64 females and 54 males, with varying periods of hyperpyrexia at 106.7° F. lasting from 5 to 17 hours. Cultures from 80 per cent of these patients became bacteriologically negative and remained so for intervals varying from one month to three years.

In the treatment of gonorrhoea of the female pelvis, the use of fever therapy combined with either diathermy to the pelvis or the Elliott treatments may be more effective than fever therapy alone. By the combined method of fever therapy and pelvic heating, one or two less treatments are necessary than with fever therapy alone. This method was developed by Bierman and Horowitz⁶ when they found it difficult to secure a cure in some of their female patients.

Gonorrheal Arthritis: In gonococcal arthritis, the results of fever therapy have been unusually good. Hench⁷ stated that after treatment with artificial fever, 70 per cent of the patients who had gonorrheal arthritis were free from symptoms and also regained complete function. An additional 10 per cent were markedly relieved and the remaining 20 per cent were unimproved. Whenever the surfaces of the joint have been destroyed and the synovial membranes have become thickened, complete restoration of joint movement can scarcely be expected. Hench's work indicates that the earlier in the course of the arthritis the treatment is given, the greater is the opportunity for complete subsidence of the infection and for almost complete restoration of articular function.

Syphilis—Early, Primary, and Secondary: It would seem that artificial fever therapy combined with chemotherapy affords better results than can be obtained by the use of either alone. In a recent article by Neymann, Lawless, and Osborne⁸ 14 patients with early syphilis were treated with hyperpyrexia. This was combined with neoarsphenamine and bismuth salicylate in seven instances. All the seven patients treated with hyperpyrexia alone had further clinical or serologic evidence of syphilis after treatment ceased. All seven patients given the combined therapy became serologically negative and showed no clinical signs of syphilis for periods ranging from five to eighteen months after treatment ceased. Simpson⁹ secured similar results in the treatment of 26 patients, all of whom were observed for six months to two and one-half years. His findings suggest that the logical time to institute combined fever-chemotherapy is immediately following the establishment of the diagnosis of syphilis.

Dementia Paralytica: Artificial fever has been used in the treatment of a total of 809 patients with general paresis as reported in the literature³. Of this number 226, or about 28 per cent, have had a complete remission, while 279, or 35 per cent, are reported as improved and are now for the most part said to be no longer in need of hospitalization. Twenty have died as a direct result of treatment. This is approximately 2.5 per cent.

Other methods of treatment of this condition bring about a rate of remission and good clinical improvement in approximately 30 per cent of the cases. During and just following the course of treatments with malaria, the death rate ranges between 10 and 30 per cent.

Tabes Dorsalis: It is necessary for more time to pass before it can be said that the progress of this disease has been arrested. Tabes, however, presents one dominant set of symptoms by which the arrest or progress of the disease can be judged—tabetic crises and lancinating pains. Hyperpyrexia has given permanent relief of these two symptoms. Ninety cases are reported in the literature³ and 60 per cent of these patients have shown clinical improvement for the most part in the cessation of crises and pains.

Cerebrospinal Syphilis: The endarteritic, gummatous, and meningitic forms of tertiary syphilis usually respond to antisyphilitic therapy. However, this form is occasionally resistant to ordinary treatment. Hyperpyrexia extends definite hope to patients suffering from tertiary syphilis of the central nervous system who have not been helped by the older and more conservative forms of antisyphilitic therapy^{3,9,10}.

Syphilitic Optic Atrophy: Neymann³, Beerman, Hirschfeld, Epstein and Paul¹¹ and others are of the opinion that no striking results have been obtained by the use of hyperpyrexia in this condition.

Culler¹², working with Simpson, reported the results secured in the treatment of 58 patients with various manifestations of ocular syphilis. He used the combined fever-chemotherapy technique of Simpson and his results show that some forms of ocular syphilis, particularly interstitial keratitis, syphilitic exudative uveitis, and choroiditis, respond well to this form of therapy.

Chorea: Artificial fever was first attempted in the treatment of this condition in 1929 when it was noted that a child improved after a fever developed following the administration of a sedative. Later, injections of typhoid vaccine for the purpose of elevating the temperature were used. This, however, frequently caused severe illness and occasionally death.

Hench⁷ has collected approximately 30 cases in the literature in which artificial fever has been used. The results vary from improved

ARTIFICIAL FEVER

to "cured"; generally they are favorable. Three patients are reported as having had a recurrence.

Asthma: It has frequently been observed that fever associated with infectious diseases often temporarily and occasionally permanently controls the symptoms of allergic disease. It occurred to Feinberg¹³ that the production of fever by artificial means might be of value in the treatment of chronic asthma and other allergic conditions.

In 1935, 117 patients were treated by this method². The results were favorable in 104 cases, unfavorable in 10 cases, and slight and indifferent in at least three other cases.

Phillips¹⁴ has used hyperpyrexia extensively in the treatment of bronchial asthma. He used it in more than 250 patients with an observation period ranging from 6 months to 3 years. Included in the group are patients of practically all ages—4 to 72 years—and both sexes are about equally represented. All types and durations of disease are included from the standpoint of chronicity, allergy, and pathology. In conclusion, he states that his results definitely indicate that fever therapy by physical means as a specific in the treatment of bronchial asthma will be disappointing and of no value except as a temporary measure, especially for breaking up an acute paroxysmal attack. On the other hand, when used in conjunction with other measures, it becomes one of the most valuable adjuncts in therapy.

Because of the severity of this treatment, fever therapy should not be attempted unless all other means have failed.

Chronic Arthritis: The clinical subdivisions of this disease are somewhat vague and ill defined; consequently there is a great deal of uncertainty and confusion about the classification. Most clinicians distinguish between two major types commonly designated as chronic, infectious, atrophic, proliferative or rheumatoid arthritis, and chronic senescent, hypertrophic, degenerative, or osteo-arthritis.

The latter group does not react well to this treatment; in fact, hyperpyrexia often makes the symptoms more severe.

The chronic infectious types respond best to hyperpyrexia if treatment is instituted early. Of this group, from 15 to 30 per cent of the patients are greatly benefited, another 30 per cent experience some relief, and between 40 and 55 per cent are not helped at all³.

Other Diseases: Favorable reports appear in the literature on the treatment of the following diseases by artificially induced fever: multiple sclerosis, Parkinson's syndrome following lethargic encephalitis, undulant fever, malignancy, corneal ulcers, and iritis.

Contraindications to Artificial Fever: Contraindications to the use of fever therapy will vary according to the elevation of temperature

needed and also according to the general physical condition of the patient.

Every patient should have a thorough physical examination and clinical investigation. The following laboratory studies should be made: electrocardiogram, complete blood count, sedimentation time, and, if the patient is suffering from infectious and gonorrheal arthritis, he should have a thorough roentgen examination. Any other procedure necessary for complete and definite diagnosis should be made.

Advanced age is usually considered a contraindication for fever therapy. However, patients from two to seventy-five years of age are reported in the literature. Patients with advanced pulmonary tuberculosis, renal or cardiac disease should not be subjected to fever therapy. Any contraindication to major surgery is likely to be a contraindication to fever therapy.

Artificial fever should not be attempted as an office procedure. It should be done in a hospital or clinic where trained technicians are available and under the direction of a physician trained in this work.

REFERENCES

1. NEYMANN, C. A. AND OSBORNE, S. L.: Artificial fever produced by high frequency currents; preliminary report, *Illinois M. J.*, 56:199-203, (September) 1929.
2. KRUSEN, FRANK H.: The present status of fever therapy produced by physical means, *J.A.M.A.*, 107:1215-1220, (October 10) 1936.
3. NEYMANN, CLARENCE A.; Hyperpyrexia produced by physical agents, Chapter 17, *Principles and Practice of Physical Therapy*, Hagerstown, Maryland, W. F. Prior Co., Vol. 1, 1933.
4. DESJARDINS, A. U., STUHLER, L. C., AND POPP, W. C.: Fever therapy for gonococci infections, *J.A.M.A.*, 106:690-699, (February 29) 1936.
5. CARPENTER, C. M., BOAK, R. A., MUCCI, L. A., AND WARREN, S. L.: Studies on physiologic effects of fever temperatures; thermal death time of *Neisseria gonorrhoeae* in vitro with special reference to fever temperatures, *J. Lab. & Clin. Med.*, 18:981-900, (July) 1933.
6. BIEMAN, W. AND HOROWITZ, E. A.: Treatment of gonorrhea in female by means of systemic and additional pelvic heating, *J.A.M.A.*, 104:1797-1801, (May 18) 1935.
7. HENCH, P. S.: Clinical notes on results of fever therapy in different diseases; report of fifth annual Fever Conference, Dayton, Ohio, May, 1935, *Minnesota Med.*, 19:151-157, (March) 1936.
8. NEYMANN, C. A., LAWLESS, T. K., AND OSBORNE, S. L.: Treatment of early syphilis with electropyrexia, *J.A.M.A.*, 107:194-199, (July 18) 1936.
9. SIMPSON, W. M.: Artificial fever therapy of syphilis, *J.A.M.A.*, 105:2132-2140, (December 28) 1935.
10. REDEWILL, F. H.: One hundred and thirty-five cases of Wassermann-fast and neurosyphilis treated with diathermy and modern medication, *Urol. & Cutan. Rev.*, 37:367-377, (June) 1933.
11. BEERMAN, W., HIRSCHFELD, M., EPSTEIN, N. N., AND PAUL, S. B.: Neurosyphilis—its treatment with hyperpyrexia produced by diathermy, *California & West. Med.*, 40:177-184, (March) 1934.
12. CULLER, A. M.: Artificial fever therapy in cases of ocular syphilis, *Tr. Sect. Ophth., A.M.A.*, 308-331, 1935; also *Arch. Ophth.*, 15:624-644, (April) 1936.
13. FEINBERG, S. M., OSBORNE, S. L. AND STEINBERG, M. J.: Sustained artificial fever in treatment of intractable asthma; physiologic and therapeutic considerations, *J.A.M.A.*, 99:801-806, (September 3), 1932.
14. PHILLIPS, K.: Hyperpyrexia in bronchial asthma, *Arch. Phys. Therapy*, 17:282-288, (May) 1936.