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Breaking the thermal barrier: Dr. Temple Fay

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Dr. Temple Fay (1895—1963), one of the most talented and skilled neurosurgeons of his time, is also considered a pioneer in therapeutic hypothermia. He was an inquisitive thinker who encountered multiple difficulties experimenting in such an unknown field. Fay believed that body temperature was an important physiopathological factor in certain diseases such as cancer. He conducted several clinical trials and broke ''the thermal barrier''. The vast majority of Fay's patients with terminal diseases experienced beneficial outcomes after ''refrigeration'' and the mortality rates were low. The cooling methods he implemented form the basis of the methods we use today to induce hypothermia. Dr. Fay's discoveries led to today's indications and techniques for therapeutic hypothermia.

Dr. Temple Fay, since the age of 12, knew where he was heading, followed his mentors and became one of the most talented and skilled neurosurgeons of his time.[1,2] His endless questions and thirst for knowledge led him to breakthroughs in several areas in neurosurgery and science, seeking for new and innovating ways for treatment through his research.[1] Like many geniuses in history, he was ahead of his time and was not fully recognized by his peers, sometimes confronting harsh criticism and isolation.

Temple Fay is remembered for several achievements but one of them makes him standout.[3] He was a pioneer of what we now know as therapeutic hypothermia, a recognized medical procedure nowadays, but an unexplored field in Dr. Fay's time. He, nevertheless, was an unconventional man, breaking barriers of time,

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prejudice, thought and most of all, temperature.[3]

His beginnings

Temple Fay was born on January 9, 1895 in the city of Seattle. His parents both came from families of great scientists and naturalists. As a child, Fay was brought up in an environment of academic achievement and high expectations.[2,3]

Fay was pressurised by his family to go into the clergy but he was set on becoming a doctor.[2] He attended the Medical School of the University of Pennsylvania.[3] Fay spent all his free time on the wards with Dr. William G. Spiller and Dr. Charles H. Frazier, who were well known as a neurologist and a surgeon respectively.[2,3] He began as Dr. Spiller's assistant and later he assisted Dr. Frazier in surgeries to become assistant in neurological surgery and instructor in neurology.[3] He learned everything he could from his mentors and became a neurologist and neurosurgeon of outstanding skill. He always demanded perfection from the people around him as well as loyalty and honesty.[2]

In 1929, he became a professor of neurosurgery and head of the department at the Temple University.[2] In 1931, he founded the Harvey Cushing Society with doctors Van Wagenen, Glen Spurling and Eustace Semmes, which, years later, became the American Association of Neurological Surgeons.[2] Dr. Fay was the Society's sixth president (see Figure 1).

His early work

Dr. Fay's interests, in the 1920s, were mainly focused on water balance and metabolism, particularly applied to reducing intracranial pressure.[1–3] In patients with intracranial hypertension, he would use hypertonic solutions, especially magnesium sulphate which could be given orally or rectally. Then remove by lumbar puncture as much spinal fluid as possible and restrict fluid intake.[2–4] These dehydrating measures were also applied to patients with migraine and epilepsy.[1–3] The same principle was applied in eclampsia, with a therapeutic modality named Arnold-Fay in 1930.[2,5]

He considered his research on biochemical and biophysical balances at the cellular level of the central nervous system to be the most important contribution of his life.[3]

He invented and modified several surgical instruments and ventured into new surgical procedures.[3]

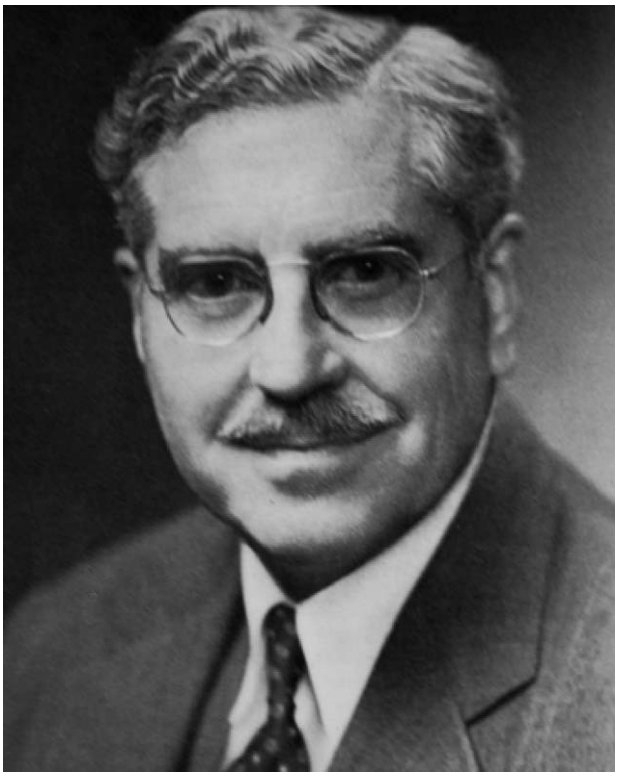

Figure 1 Dr. Temple Fay.

In 1923, he developed, with Dr. Francis C. Grant, a ventriculoscope which could be adapted for intraventricular photography.[1,2,3,6] He elaborated on an instrument which combined suction and irrigation for intracranial surgeries.[3,7] He was one of the first surgeons to approach neuralgia of the glossopharyngeal nerve with an intracranial approach.[1,2,3,8]

Breaking the thermal barrier

While Dr. Fay was still in medical school, he participated in a knowledge quiz. Directing the quiz was Dr. Allen Smith who asked Fay if he knew why metastatic cancer rarely appears in the limbs.[3] He answered that he did not know and his professor acknowledged he did not know either; this question would leave a great impression in Fay's mind.[3]

In the late 1930s, he finally decided to pursue the answer to this question and started his research on the matter. He hypothesized that the differences in the location for cancer growth had to do with temperature and soon started collecting data of temperatures at different body sites.[2] He used a thermocouple device and a galvanometer determining variations of segmental or dermatomal

temperature elaborated by George C. Henny of the Department of Biophysics at Temple University.[3,9] He found a decrease in temperature of 12—22 °F below knees and elbows compared to the rest of the body.[3,10] In contrast, he observed that common cancerous sites, were mostly located in areas with higher temperatures.[3,10]

Fay also investigated the effects of different temperatures in chicken embryos at his farm in Maryland.[3] With the assistance of Dr. Lawrence W. Smith from the Department of Pathology at Temple University, he found a marked retardation and inhibition of embryonic growth with the use of low temperatures as he discovered that cellular differentiation seemed to cease almost entirely at 90 °F.[10] Dr. Fay determined that cellular temperature levels were a factor in the evolution of cancer cells.[2,10] He found through tissue culture methods that the growth of tumor cells was affected by temperature.[2,10]

The next step was to apply this in the clinical setting.[10] He was the first physician ever to perform ''cooling'' trials on humans. Patients with terminal, inoperable cancers were treated with local ''refrigeration'', as he would call it.[10,11] Local refrigeration was reached with the application of ice water and ice at first.[10] The first attempts included a water cooler, rubber tubing and a discarded CO_2 gas capsule with two small metal tubes soldered into its neck.[12—14] Later on, Fay implemented cooling devices designed individually using coils, hollow metal capsules or appropriately fitted rubber bags to fit the structures in which the tumors were located and to secure the maximum distribution of cooling process (see Figure 2).[10,12,13]

The first reported patient of Dr. Fay to undergo hypothermia (July 1936) was suffering from intractable pain from massive pelvic extension of a cervical carcinoma.[10] The capsule, connected to a continuous circulation of ice water, was inserted deep in the vaginal mass and continuous refrigeration of the local area was maintained by constant circulation of water through an enclosed system at approximately 36 °F.[10] At the end of 48 h, the patient was pain free. Within 5 days, the carcinomatous area had definite devascularization and shrinkage of the gross mass.[10]

In cases in which Dr. Fay wanted to implement hypothermia into deep areas of the body, mainly the brain, he used local implants of subfreezing metal capsules or ''bombs''.[14] These capsules with connecting tubing were sterilized and introduced into the brain through a trephine or craniotomy adjacent to the lesion.[14] The results in patients with cerebritis, osteomyelitis, skull fractures or after neurosurgical removal of the necrotic core

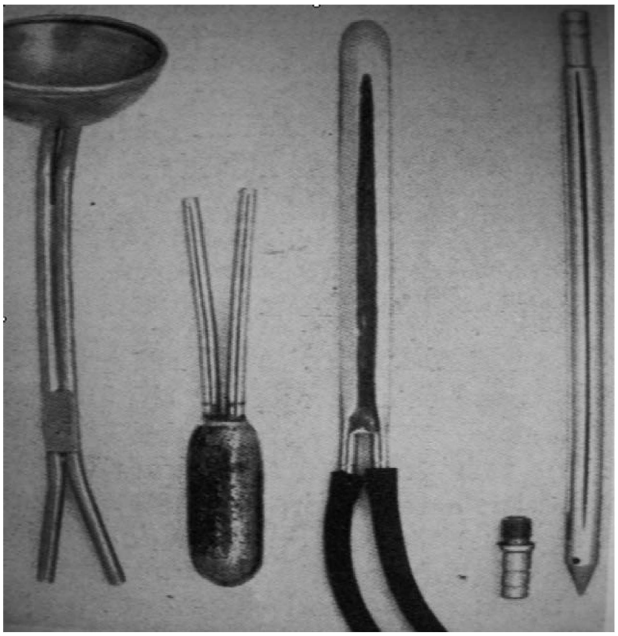

Figure 2 Instruments used by Dr. Fay for ''local refrigeration''.

of gliomata were very encouraging.[14] Fay noticed a reduction in pain and swelling in the area of trauma or infection, as well as a bacteriostatic effect. This approach was used before antibiotics were available.[14]

Dr. Fay continued to perform local refrigeration and serial biopsies at varying intervals in several patients with carcinomatous lesions near body surfaces. It became obvious that local hypothermia, when applied to involved areas, promptly controlled pain, retarded malignant cellular metabolism and growth, was bacteriostatic, reduced inflammation and was well tolerated by the brain.[14] Dr. Machteld Sano from the Department of Neuropathology established the critical level of temperature for division of malignant cells in vitro.[14] This critical level was reached at 67.5 °F.[14]

The following question naturally arose as to the possibility of reducing the entire body temperature below the ''normal level'', in hopes of retarding the growth of deep metastatic tumors inaccessible by local hypothermia methods.[14] It was also intriguing to know how far it would be safe to carry the body temperature below the standards of ''normal'' and for how long.

The first attempt of general ''refrigeration'' was made on November 28, 1938.[14] It was a cool crisp day and Fay opened the window in the patient's room and shut off the heat. One hundred and fifty pounds of ice chips were placed over the patient as he lay in bed.[14] Soon after the patient received sedation and her body temperature dropped to the

low 30's °C.[14] Clinical hypothermia was experimentally achieved that afternoon.[14] The patient's blood pressure and pulse virtually disappeared, and although the patient continued to breathe, the fear of cerebral hypoxia persisted.[14] The patient was rewarmed to normal temperature values again with heat applied to body surfaces and a hot coffee enema.[14] Within a few hours, the patient had returned to conscious levels and was not aware of the experience.[14]

The majority of Dr. Fay's early hypothermia patients were physicians or nurses who understood the inevitable outcome of metastatic malignancies.[14] Each patient was prepared differently before inducing hypothermia.[14] Each individual's personality and emotional state were evaluated closely at least 18—24 h before the induction of ''refrigeration''.[14] Most patients received chloral hydrate and sodium bromide by mouth or rectum the night or the morning before the induction.[14] Moments before the period of actual ''refrigeration'', paraldehyde was given.

Fay believed that the fact that the patients knew the truth about their terminal condition gave them a new found self-confidence.[14] He believed every patient had to be ready before initiating hypothermia rather than rushing them to fit into the schedule of the hospital.[14] When the patient's body temperature began dropping beyond 33 °C, pulse pressure, hemoglobin, pH and CO_2 determinations, urine and blood analysis were monitored regularly.[14]

The nursing staff at first was quite concerned about working in the ''Refrigeration Service''.[14] The nurses had difficulties getting the patient's temperature with the long-stemmed laboratory thermometers, difficulty getting the readings for the blood pressure, and water and ice were everywhere in the room.[14] The programme was almost shutdown when some nurses started getting ''colds'' and other illnesses.[14] Fortunately, special blankets made of rubber tubes devised to carry a cold solution from a special ''beer cooler'' machine pumps were commercially available and were found to be useful in this technique (see Figure 3).[14] Electric thermocouples for 24-h charting of rectal temperatures were also designed. The need for cold rooms disappeared with the use of this apparatus and no further complaints were received from the nursing staff.[14]

The preliminary results of Dr. Fay's program were presented at the Scientific Session and Exhibit of the American Medical Association in St. Louis in 1939.[14] Even though the potential of ''refrigeration'' was evident in many aspects, his work received a ''cold reception''.

Figure 3 Patient in ''general refrigeration'' with the help of a special blanket containing rubber tubing, continuous circulation of chilled solution and automatic temperature control. Picture also shows rectal thermocouple.

During World War II, the Germans apparently captured one of his manuscripts, 'Observations on Prolonged Human Refrigeration', sent to Belgium for publication and became familiar with the technique. Refrigeration was used experimentally in concentration camps and became an infamous procedure.[14] This was thought to delay the progress of hypothermia for about 10 years.

From July 9th, 1936 to October 1st, 1940, Fay conducted 169 episodes of ''refrigeration'' treating a total of 126 patients, mostly with terminal cancer (112 patients), five patients with brain tumors, four with leukemia, three with Hodgkin's disease, one patient with filariasis and another one with syphilis.[12] In 83 instances, the patients were treated with local ''refrigeration'' maintained at 7 °C.[12] In 66 patients, general ''refrigeration'' was induced from 12 to 24 h to 8 days, ranging rectal temperatures from 33 to 25 °C.[12]

The most remarkable effect of hypothermia in these patients was the relief of pain that the vast majority of the patients experienced.[11,14] The basal metabolism was reduced on average by 20—25%.[11] Acute anemia was noted in some patients who underwent several periods of generalized refrigeration. In the first 24—48 h, a number of patients experienced a rise in the leukocyte count of 15—20,000 with a normal differential count. A drop in the urea levels and blood sugar was also seen in some patients. Kidney function was noted to be maintained if intravenous fluids were provided.[11]

Repeated neurological examinations were also performed in 42 of the patients subjected in all to 83 episodes of refrigeration with the assistance of Dr. Gerald W. Smith.[13,14] Each period varied in

duration from 24 h to 5 days and a total of 400 examinations were performed.[13] Increase in deep tendon reflexes was seen at a temperature range of 36—30 °C which corresponded to the shivering stage. Abolition of deep tendon, abdominal and gag reflexes occurred at 25 °C. The pupils remained equal, regular and normal in size but the response to light became progressively sluggish until it was abolished at 25 °C. Dysarthria began at 35 °C and retrograde amnesia remained below 35 °C. Cerebration was delayed and mental faculties were preserved until the temperature reached 35 °C. The relief of pain was seen in 95.3% of the patients.[13]

As happens to most innovators, Dr. Fay was roughly criticised by his peers since at that time the general understanding was that survival below 35 °C was impossible.[3,14] All the clinical thermometers were calibrated down to only 35 °C, the lowest temperature compatible with human life.[14]

Dr. Fay always acknowledged the use of refrigeration as an ancient art.[14] In the clinical setting, scientists such as Thomas Bell (Bell's palsy) (1829), John Hughes Bennett (1849), James Arnott (1851), Thomas Weedon Cooke (1865), J.W. Bright (1871), and S. Weir Mitchell (1872), reported favorable results in a variety of clinical conditions.[14]

The last article Fay published, in 1959, looked back to his earlier studies in hypothermia and acknowledged the group of courageous young people who worked with him.[14] He felt ''fortunate, because when one strays from the conventional paths of medicine, there is a great comfort and encouragement in the assurance and confidence of the younger minds to offset the disapproval and outright condemnation from the older and more conventional members of the profession''.[3,14] It was then, and not 20 years before, that he could now talk about human refrigeration to most of his colleagues without the criticism and antagonism of the past.[14]

His last days

Dr. Fay's last years of clinical research were focused on studying mental paralysis and rehabilitation.[1] In 1960, after developing hypertensive encephalopathy, he spent his last few years at his home close to a small nucleus of family and friends, continuing to study and write, still looking ahead.[2,3]

Therapeutic hypothermia has become part of the armamentarium for clinicians over the past 5 years.[15—17] Use of this technique has clearly shown significant neurological improvement in a variety of settings.[18,19] This improvement is mainly due to Dr. Fay's efforts at breaking the thermal barrier and many others that worked in this field.[20]

Conflict of interest

The authors disclose no conflict of interest in the preparation of this manuscript. The article is not biased towards any of the authors' opinion and in no way was written with the intent to persuade the audience towards any particular point of view. The authors did not receive any compensation or grant to elaborate this manuscript.

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