HYPOTHERMIA IN THE TREATMENT OF CRANIOCEREBRAL TRAUMATISM

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(Received for publication April 16, 1957)

The treatment of cranio-cerebral injuries has been improved considerably during the past twenty years thanks to the development of new techniques of examination, a better understanding of the possibilities and indications for surgical intervention and the correction of neurovegetative derangements and of respiratory and metabolic disturbances. However, there are still unsolved problems in this field and perhaps therapeutic hypothermia may provide the solution for some of these. Since the end of 1951 we have treated patients with cranio-cerebral injury with hypothermia. This form of treatment was created in 1941 in the United States by Fay and reintroduced in France by the authors in a different form, inspired by Laborit and Huguenard. It has often been criticised but has been adopted by many.

I. THE PROBLEMS THAT ARE RAISED

1. Anatomicopathological Data. The traumatism produces lesions about which reactions develop. The different phases of this process follow each other and are interwoven. The reparatory phase, not always achieved, follows the others.

The lesions are seldom unique and limited, but on the contrary are usually multiple and dispersed through different levels.

The perilesional reactions, often extensive and durable, play a part in the evolution of the disease which is often important and lasting. They are by definition reversible, if treated early. If they are prolonged they result in irreversible secondary lesions (epilepsions) which may cause death. (a) The reactions at the cellular level are associated with a hypercatabolism of the proteins and hydrocarbons, a hyperpermeability of the cellular membranes with a loss of potassium from the cells and a retention of hydrosodium. (b) The vasomotor reactions may produce a local asphyxia followed by vasodilatation and vasoplegia, hyperpermeability of the capillaries and diapedesis. Vasomotor disturbances tend to extend like a spot of oil and often end in generalized vasomotor disturbances with serious reactions in the brainstem. (c) The general cerebral reactions develop from the interstitial edema produced by the vasodilatation, with extravasation of plasma and variable degrees of cellular infiltration.

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The intracranial hypertension is at first compensated for by the squeezing out of cerebrospinal fluid and of intracranial venous blood. Soon a vicious circle develops when herniations of the temporal or occipital regions appear. These compress the brain stem, block the fluid pathways and produce venous stasis, thus aggravating the edema. Compression of the cerebral arteries causes ischemia and cerebral anoxia is the terminus.

Irritation of the brain stem is the common denominator of all of the preceding phenomena. The brain stem may suffer directly from the initial trauma and again from compression produced by the intracranial hypertension and the herniation. It in turn affects the entire organism unfavorably.

2. Clinical and Humoral Data. The vegetative disturbances evolve in two phases: A vagal phase, often unperceived because it is short, follows the traumatism immediately. The patient is pale, hypotensive, bradycardiac, bradypneic and easily hypothermic. It may be associated with the discharge of acetylcholine described by Bornstein. A hypersympathicotonic phase follows it; the patient becomes febrile, hypermetabolic, hyperpneic, tachycardiac, etc. The reactional nature of the clinical picture is evident. The respiratory and circulatory disturbances, the visceral dysfunctions, renal in particular, even the acute pulmonary edema and antemortem hemorrhages in the digestive tract are expressions of the irritation of vegetative centers. Protein hypercatabolism is evidenced by an increase in urea in the blood and urine. The escape of cellular potassium results in a negative potassium balance, while the entry of sodium into the cells is revealed by a hyponatremia without hypernatruria.

The systemic phenomena resulting from the cerebral troubles contribute in turn to their aggravation. The hypoxia and hypercapnia increase the cerebral vasodilatation together with the arterial hypertension. Coma is a superadded cause of metabolic disturbances. The elevation of temperature increases central sympathetic excitability.

As the lesions from which these patients die are often secondary to the reactions, therapy must be antireactional and prophylactic in preventing secondary lesions. Toward this end our treatment should be so directed as (1) to diminish cellular metabolism and if possible to restore potassium to the cells; (2) to inhibit vegetative reactional and endocrine systems; (3) to restrict intracranial hypertension and (4) to increase cerebral resistance to anoxia. In this sense hypothermia seems to be a logical form of treatment from many points of view.

II. HOW HYPOTHERMIA RESOLVES THESE PROBLEMS

Two series of observations, one from North America and one from France, have led to this form of treatment.

(1) Some investigators have induced a deep hypothermia (30°C.) by means of intense refrigeration, rendered tolerable by narcosis. Hypothermia lowers general metabolism (to 50 per cent at 30°C. to 30 per cent at 25°C.), lowers cerebral metabolism and increases the resistance of the brain to hypoxia. This has been demonstrated by Lougheed and Kahn, Botterell
According to Lougheed and his collaborators it also diminishes intracranial hypertension, arterial and venous tension, the secretion of cerebrospinal fluid and the reactivity of the reticular formation. The arterial and cerebral hypotensions produced by hypothermia are more efficacious than those obtained with the true ganglioplegic drugs (methonium, thiophanium, etc.). With hypothermia a decrease in metabolism precedes the lowering of pressures (curve of Bigelow), whereas with the true ganglioplegics the lowering of the arterial tension occurs without any previous fall in metabolism. With the exception of the tentative experience of Fay4 deep hypothermia without narcosis has not been applied to the treatment of cranial traumatism, to our knowledge.

(2) The authors, following Laborit’s6 investigations, have used less hypothermia associated with a neuropletic to obtain vegetative inhibition, and with endocrinological medication.

The drugs used are central neuromoderators (derived from phenothiazine, Rauwolfa, procaine, etc.), sympatholytics (chlorpromazine, Hydergine, procaine, etc.), parasympatholytics (diethazine, piridosal, etc.), antihistaminics, and the anabolic hormones (somatotrophic hormones, androgens, mineral corticoids). They are employed conjointly. Potassium must usually be given. The neuropletics facilitate the induction of hypothermia and avoid shivering. They also lower both general and cerebral metabolism and augment the resistance to hypoxia. The sympatholytic and parasympatholytic drugs combine to assure an equilibrated vasomotor blockade. They also have an anti-edematous action and inhibit the reticular formation.

The neuroplegia by itself ameliorates the hyperthermia, respiratory difficulties, etc. without lowering dangerously the level of consciousness. Certain drugs, especially chlorpromazine, favor the entry of potassium into the cells. The therapeutic efficacy of these drugs is so great that some authors have advised utilizing them without using refrigeration.

For the most part refrigeration is produced by conduction, i.e. by placing the patient in contact with a cold body—vessels or mattresses containing ice or covers with cold water circulating through them. However, we prefer to produce refrigeration by convection, i.e., by the transmission of heat to the surrounding refrigerated air. The “atmospheric hibernator” of Laborit is a tent ventilated with air cooled to 15°C. The chambers that we have had constructed have a current of air regulated progressively from 22°C to 12°C. The humidity is maintained between 30 and 65 per cent. The degree of hypothermia obtained varies from a restoration of normal temperature to a lowering of general body temperature to 30° to 34°C.

III. OUR RESULTS

In a series of 670 patients* with craniocerebral injury 47 have been subjected to hypothermia under neuropletics, i.e., 7 per cent. They were suffering from such severe neurovegetative disturbances that their death was

* Our service receives only patients with the most serious craniocerebral injuries.
regarded as imminent. They were deeply comatose, had a stertorous polypnoea (frequently with cyanosis) and generally an increasing fever which had already attained 39° or 40°C. All except 8 were tachycardiac; none was bradycardiac. In at least 5 cases there was black vomitus. The signs indicative of injury to the brain stem were decerebration, asynergia of the eyeballs, and bilateral Babinski sign. Cases of lesser gravity, in which patients were treated with neuroplegics without hypothermia, are not considered here.

Of the 47 patients reported here (Table 1), 13 were operated upon and in all but one an extradural or subdural hematoma was found.

**TABLE 1**

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Thirteen patients (27.7 per cent) survived. Thirty-four (72.3 per cent) are dead. Of the 13 who survive, of whom 3 were operated upon, 9 regained complete health. One suffered loss of consciousness for 2 months and then regained consciousness slowly. He had pressure sores, paralysis with contractures and a psychic deficit. Two others had psychic disturbances and one had a transitory diabetes insipidus.

Of the 34 who died, 10 were operated upon. Ten (21.2 per cent) were dead at the beginning of treatment, sometimes even before it had time to act. In half of these, nevertheless, a transitory amelioration (arrest of the rise of temperature and improvement in respiration) occurred. Three patients only (6.3 per cent) died on the second or third day during treatment. Death was always preceded by some improvement coincident with the drop in temperature. Ten patients (21.2 per cent) died shortly following the termination of treatment. Most of them had improved transitorily, some had become able to swallow, a few recovered consciousness. Later their condition deteriorated and further treatment was without effect. Eleven (23 per cent) died later, 3 to 4 weeks after treatment. Most of these had remained in a precarious condition, unconscious and unable to take nourishment.
Autopsies were obtained in 20 of the 34 deaths. In 18 cases there were deep-seated hemorrhages and grave cerebral lesions. In 2 cases only a simple edema with temporal herniations was found.

DISCUSSION

Treatment with hypothermia and neuroplegia is effective against the acute post-traumatic neurovegetative syndrome, except in those cases in which the patients are so critically injured that they die in the first few hours. Other patients show a definite improvement coincident with the induction of hypothermia which is spectacular and almost constant. Unfortunately this improvement is often temporary. After the termination of treatment the vegetative disequilibrium often recurs and many of the patients die rather promptly. Others continue on in a vegetative state of psychic and physical inertia which seems to be the expression of destructive lesions of the diencephalic nuclei. The cachectic forms are the most common. A hypersomnic form has also been observed which may terminate in an unexpected recovery. Recovery can be regarded as possible if hypothermia is easily induced with an improvement in the various symptoms, as probable if the critical period of reheating is passed without a recurrence of symptoms and as certain if the patient regains consciousness at the end of the first week. The outlook is dubious in those patients whose disturbed condition becomes chronic.

Commencement of treatment late is an important cause of failure. Unfortunately, few patients came under our care in the first few hours after injury. Of the 47 who were treated with hypothermia, 24 began treatment during the first day, 6 on the second day, 3 on the third day, 5 on the 4th, 4 on the 5th, and 3 on the 8th day or later. All patients whose treatment was begun after the third day are dead. Of the 13 patients who survived, 5 began their treatment in the first few hours, 5 during the first day and 3 on the third day. It thus appears unwise to wait until the vegetative symptoms are clear or alarming before beginning treatment. Furthermore, the induction of hypothermia is easier during the vagal phase immediately after injury than it is during the hypersympathicotonic phase which follows it.

There are few contraindications. Shock is not one of them; in fact, it is benefited by neuroplegia and hypothermia with blood transfusion. Multiple injuries are not a contraindication. The principal handicap in this form of treatment is the lack of necessary equipment and of adequately trained personnel.

It has been said critically of this form of treatment that one is complicating coma with induced sleep. However, experience has shown us that the induction of profound sleep renders the coma less profound in a few hours, rather than aggravating it. The neuroplegics that are not hypnotic (Hydergine, procaine, etc.) have the same effect. The neuroplegia and hypothermia do not mask the neurological signs as was first feared. The semiological modifications are slight. In fact clinical investigation is facilitated. The danger of ventricular fibrillation does not exist with the rather slight degree of hypothermia that we have used. On the other hand, the improvement re-
sulting from hypothermia may sometimes be deceptive. One must remain vigilant for operable lesions. The need for complementary examinations such as arteriography is not lessened. Neither is hypothermia an exclusive therapy, merely an excellent basal one. Constant attention must be given to the need for tracheotomy or artificial respiration and to the renal, metabolic and nutritional needs of the patient.

Many workers are agreed as to the basic principles of the treatment of severe craniocerebral injuries by hypothermia but there is less agreement as to technique. Some prefer hypothermia without neuroplegia; others think neuroplegia sufficient; while others, including the authors, prefer a combination of moderate hypothermia and neuroplegia. Neuroplegia increases the lowering of metabolism and has a specific effect on post-traumatic reactions. It facilitates hypothermia as much as narcosis does but in a better way. It is preferable to narcosis in unconscious patients (still sensible to cold and apt to shiver) as it does not greatly deepen the level of unconsciousness. And it may be continued for several days, if necessary, without disadvantage.

Our present techniques are not without defects. The induction of hypothermia is slow. The period of metabolic instability may not be passed until a frank hypothermia (at least $34^\circ$C.) is reached. The North American methods of refrigeration appear to act more quickly so that a hypothermia of $30^\circ$C. and a reduction of the metabolism by half is achieved within 2 hours.

It is suggested that the best results will be achieved with a combination of neuroplegia and moderate refrigeration. Deep narcosis, which has been shown to be useless, should be abandoned. The induction of hypothermia should be quickened. Practice will improve our efficiency and bring the progress which is still needed.

REFERENCES*


* A more extensive list of references will be found in *L’hypothermie dans le traitement des traumatismes crânio-cérébraux* by G. Lazorthes and L. Campan, to be published in the Proceedings of the First International Congress of Neurosurgery (1957), Brussels, Belgium.