

ARTIFICIAL HIBERNATION

Technic, and Observations on Seriously Ill Patients

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ARTIFICIAL HIBERNATION attempts to duplicate the metabolic state of the naturally hibernating animal which during winter sleep seems to be very resistant to serious injury, including temporary arrest of the circulation, and to infection. At the approach of winter, the maple tree loses its leaves; the lizard disappears to sleep; some warm-blooded animals, like the ground hog, go into hibernation; but man, in the face of severe external conditions tries to protect the stability of his internal environment. Thus, when anything disturbs him, reactions of defense set in. The defense reactions often overcome the disturbing factor, but sometimes they mount to an impractical and futile fight.

In seriously ill patients, uncontrolled defense reactions, such as extreme rises in body temperature, immoderate secretion of epinephrine, excessive vasoconstriction, and increased metabolism may produce more damage and be much more harmful to the body than the aggression itself. In the disorganized struggle that follows, many patients die. The body's reaction may be dampened by hibernation, so that, like the hibernating animal, the patient can undergo the aggression without sustaining self-inflicted damage. This, at least, is the principle on which Laborit and Huguenard¹ have based their application of artificial hibernation.

Artificial hibernation establishes, for the time, a retrograde evolution that, in emergent situations, attempts to copy the status of creatures less evolved than man himself. Real hibernation cannot yet be duplicated. The fall of temperature in artificial hibernation is less; there is, moreover, a tendency to ventricular fibrillation at low temperatures which is unknown in natural hibernation.

The purposes of this paper are to review aspects of artificial hibernation reported in the European literature and also to describe our own experiences in cases in which we have followed the French technic.²

We have used this new procedure only in patients whose clinical condition was deteriorating so rapidly that, with currently available methods but without hibernation, it seemed hopeless. Our ultimate results reflect this selection; nevertheless, temporary improvement often was observed, and most of the patients were more comfortable than prior to hibernation. Our results tend to confirm those of Laborit and Huguenard, and we believe that further application in patients whose clinical condition is less critical than the ones described is now indicated.

Indications for the Use of Artificial Hibernation

Artificial hibernation has been advocated for use in general surgery in the poor-risk patient, in cardiac surgery, neurosurgery, and in obstetrics.¹ The relative value of this procedure as compared with refined anesthetic technics is hard to assess from the available reports, especially in the category of poor risks. The first reports on treatment of severe myocardial infarction in patients are favorable²; experimentally, dogs that would have died after ligation of a coronary artery, survived when this operation was performed under hibernation.³ Artificial hibernation was used for prevention and treatment of wound shock during the war in Indochina.⁴ Jaulmes⁵ compared shock resulting from bleeding in anesthetized dogs and in dogs under hibernation; he reported that the hibernating dogs withstood bleeding better and longer. The ultimate survival of these dogs, however, was not studied.

It might be asked: Of what good is prolongation of life if, during hibernation, repair of existing damage does not take place? However, a large experience¹ indicates that wound healing proceeds unimpaired. Premature and newborn children, unable to resist the aggression of a new and hostile world, continue to grow during hibernation, notwithstanding low body temperature. Insufficient data are available to judge regeneration of higher organs such as the liver and the kidney.

Artificial hibernation also has been used in the treatment of severe infections. Leucocytosis certainly is not impaired, but rather is increased. Bacterial growth is slowed though not arrested, so that antibiotic therapy should be continued as before hibernation. Artificial hibernation has been used successfully to reduce temperature in the hyperpyrexia of hemorrhagic scarlet fever,⁶ and in babies with severe infections (often in the gastrointestinal tract), a condition called "neurotoxicosis" by the French.¹

Artificial hibernation has been advocated for serious conditions in which oxygenation is insufficient because of cardiac failure, pulmonary embolism or other impairment of the respiratory system.

From the few foregoing examples, it is evident that a large field of uses for artificial hibernation is yet to be explored.

"Neurovegetative Blockade" ("Inhibition neuro-végétative; neuro-endocrinienne")

In simple refrigeration, the patient is anesthetized and subsequently cooled. The HCO_3^- -content in the blood falls when no special precautions—such as overventilation—are taken.^{7,8} The defense reactions of the body set in, and oxygen consumption is increased, at least in the beginning. Rather deep anesthesia is required to prevent shivering.

Conversely, in artificial hibernation, the patient is given a combination of drugs intended to dampen certain parts of the central and the autonomic

nervous systems.^{1,2} The blocking is said to take place at the levels of cortex, mid-brain, ganglia, and nerve endings. Moreover, the "neurovegetative endocrine" system is blocked, and reactivity to substances such as Adrenalin is said to be diminished. Thus, the constancy of the internal environment no longer is maintained. After blockade, when one leaves a patient without covering in a room of ordinary temperature, his body temperature spontaneously will go down to about 32 to 28 degrees C. (90 to 82 degrees F.). During hibernation, there is no shivering, and no increase in oxygen consumption. Laborit¹ believes that the severe, generalized vasoconstriction that occurs during the defense against aggression is injurious to the organism. Thus, he attempts to produce vasodilatation.

Drugs Used in Hibernation

To point out the importance of hibernation-drugs, Jaulmes³ listed four procedures in descending order of their protective ability against shock by bleeding; the sequence is: (1) artificial hibernation, (2) refrigeration alone, (3) administration of chlorpromazine without refrigeration, and (4) administration of ganglion-blocking agents like hexamethonium.

The most important drugs used in artificial hibernation were all developed in France by the firm of Rhône Poulenc; they are derivatives of phenothiazine: Phenergan, Diparcol, and chlorpromazine. Huguenard² listed the properties of the phenothiazine derivatives and we have transposed his list into two schematic drawings (Fig. 1). Figure 1A indicates functions and nerves that are inhibited. Figure 1B indicates functions that are enhanced. Phenergan, Diparcol, and chlorpromazine have to a certain extent similar actions, although there are differences. Phenergan for example is an antihistaminic. Diparcol is supposed to be a bronchodilator and to inhibit bronchial secretion. Chlorpromazine is by far the most important of the phenothiazines in artificial hibernation.

Additional drugs are used, as will be indicated in the section on technic, with the purpose of (1) supporting the action of the phenothiazine derivatives (Demerol hydrochloride, barbiturates); (2) reducing capillary permeability (thiamine); and (3) preventing the occurrence of intravascular thrombosis, especially during the period of rewarming (heparin). Other drugs like Hydergine, MgSO₄ and procaine are alternated with the derivatives of phenothiazine to prevent development of tolerance. The use of growth hormone also is advocated, as it is hoped to have an anabolic effect.

I am unable to assess the relative virtues of activities of the many drugs used. One is reminded of the tailor who, when blamed for having made a mistake on an expensive coat, answered in defense: "Sir, the art of tailoring has not regressed to the state of an exact science." In other words, it seems to be intuition that has guided the French. It is an approach that is widely criticized in this country; however, I think that we should reserve our judgment in this instance until we have had more experience.

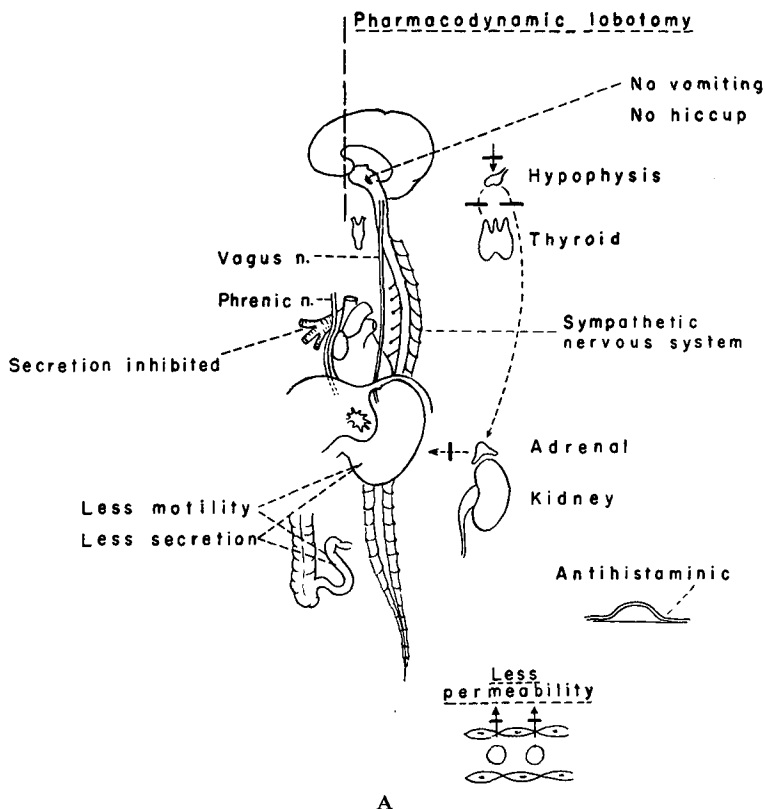


Fig. 1. Pharmacologic action of the phenothiazine derivatives: chlorpromazine, Phenergan, and Diparcol, as listed by Huguenard² and transposed into a diagram. (A) Functions or nerves that are inhibited.

Technic of Artificial Hibernation

The following technic of hibernation is based on that of Laborit and Huguenard.^{1,2} As we instituted hibernation only as a last-resort measure in very ill patients, our procedures differed somewhat from the standard French prescription.

Outline of Technic

Pretreatment: Give 50 mg. chlorpromazine intramuscularly immediately upon decision to start hibernation.

Induction: Start intravenous infusion of 5 per cent glucose in water at a rate of about 15 drops per minute. Inject into the tube every 15 minutes, 2 cc. of the following mélange:

ARTIFICIAL HIBERNATION

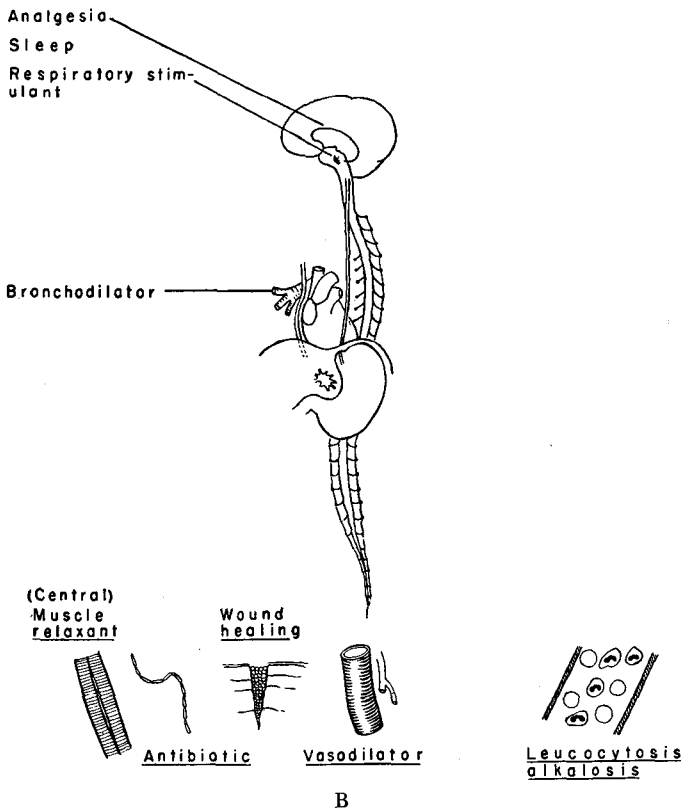


Fig. 1. Pharmacologic action of the phenothiazine derivatives: chlorpromazine, Phenergan, and Diparcol, as listed by Huguenard² and transposed into a diagram. (B) Functions that are enhanced.

Mélange No. 1

Phenergan*	50 mg.
Chlorpromazine (Thorazine**)	50 mg.
Demerol hydrochloride	100 mg.
Saline to make	12 ml.

After the last injection, which should be given 1¼ hours after the first one, refrigeration is started.

After the injection of Mélange No. 1, replace the 5 per cent glucose solution with Cocktail No. 1.

*Phenergan hydrochloride was provided by Dr. Daniel L. Shaw, Jr., of Wyeth Laboratories, 1401 Walnut St., Philadelphia, Pennsylvania.

**Thorazine was provided by Mr. Edwin Boone, of Smith, Kline & French Laboratories, 1530 Spring Garden St., Philadelphia 1, Pennsylvania.

Cocktail No. 1

Phenergan	150 mg.
Chlorpromazine	150 mg.
Demerol hydrochloride	150 mg.
Thiamine	200 mg.
Diparcol†	250 mg.
Glucose 5% to make	900 ml.

Cocktail No. 1 should be administered over a period of 18 hours (50 ml. per hour or about 12 drops per minute). Mark the specific height where the fluid level should be at two-hour intervals on the bottle with adhesive tape to insure a constant rate.

Second day:*Cocktail No. 2*

Hydergine (Sandoz)	3 ml.
(This is .9 mg. of equal parts of dihydroergotamine, dihydroergokryptine, and dihydroergocristine methane-sulfonates.)	
Procaine	3-6 Gm.
Magnesium sulfate	6 Gm. (only if renal function is unimpaired)
Thiamine	200 mg.
Glucose 5% to make	900 mg.

Cocktail No. 2 also should run 18 hours.

Third day: (Warming up)*Cocktail No. 3*

Thiamine	200 mg.
Ascorbic acid	1 Gm.
Ethyl alcohol	50 Gm.
Procaine	2-4 Gm.
Glucose 5%	1000 ml.
Normal saline to make	1800 ml.

Cocktail No. 3 should drip for 24 hours; this is at a rate of 75 cc. per hour.

Refrigeration is started after the last injection of Mélange No. 1. The patient is naked except for a "Bikini." Ice bags are applied on the axillae, on the groins and over the liver, or an electric fan is used to blow cool air over the patient to help refrigeration. Instead of ice bags, ice chips may have to be employed, or the patient may be put on a refrigerating mattress or wrapped in a refrigerating blanket through which ice water circulates. The room should be cool (windows open if it is cooler outside).

If shivering, restlessness, or other reactions occur, administer additional doses of 12.5 mg. Demerol hydrochloride alternately with 10 mg. of Nembutal into

†Diparcol was supplied by Mr. R. Deville, of Rhodia Inc., 230 Park Ave., New York 17, New York.

the tube of the intravenous infusion every ten minutes until the patient becomes quiet.

The body temperature is maintained between 32 and 34 degrees C. (between 90 and 93 degrees F.); overshooting is dangerous. Deep rectal temperatures are taken every half hour. (The rectum may be colder than the rest of the body if the patient is lying on an ice-water mattress.) Continue to apply ice when the temperature is down to 34 degrees C. (93 degrees F.) but remove it when the temperature is 33 degrees C. and the trend still is downward. Move the patient from side to side. If secretæ accumulate in the trachea, frequent aspiration should be performed or tracheotomy may be necessary.

Blood pressure, pulse, and respirations should be followed and recorded at least every half hour.

Supportive therapy. Intramuscular administration of 100 mg. of growth hormone per day and Neodrol (androstanolone) or methylandrostenediol or testosterone 50 mg. per day are given for their supposed anabolic effect; heparin 50 mg. two times per day, is continued throughout the period of hibernation. If there are no contraindications, it is wise to increase the heparin dosage to 200 mg. per 24 hours intramuscularly during rewarming.

If the hibernation must be continued over several days, Cocktail No. 1 may be continued during the second day and, Cocktail No. 2 is given on the third day; these are alternated daily thereafter.

If the patient is being allowed to warm up, administer Cocktail No. 3.

Fluid and Electrolyte Requirements

During hibernation, fluid and electrolyte requirements are less than usual. If too much water is given there is great risk of overhydration. Fluid loss by drainage from gastric tubes or other drains must be replaced. Glucose is poorly utilized; the levels of blood sugar usually are high—around 200 mg. per cent. The administration of amino acid preparations is contraindicated if renal failure is present; otherwise it seems to be advantageous. Especially during induction of hibernation when the vasodilatation occurs—the blood volume may have to be replenished with dextran or blood. In patients with renal failure, it is best to use dextran 6 per cent in 5 per cent glucose rather than the commercial dextran that comes in normal saline.

Clinical Aspects of Artificial Hibernation

A patient who is anxious, fighting, restless, cyanotic, and miserable, becomes calm after induction of hibernation; he does not complain about pain; he appears to be sleeping but does respond. Complications are not masked. He will respond if you press on a broken leg or into a painful abdomen. There never is vomiting or hiccuping. Nails, ears, and lips are pink. In cases of ileus, the

TABLE
Experience with Artificial Hibernation in Nine Patients

Diagnosis and condition before hibernation. Age, sex	Indication for hibernation					Duration of hibernation	Additional therapy		
	High temperature	Low blood pressure	Ileus	Uncontrollable deterioration	Other factors		Artificial kidney	Tracheotomy	Other
1. <i>Traumatic pancreatitis</i> , crush syndrome, fractures, uremia. 34 yr. M	+	+	+	+	Restlessness	6 days	+	+	Craniotomy, cystoscopy
2. Aortic graft, <i>ischemic necrosis</i> of kidney, uremia. 57 yr. M	+			+	Convulsions	2½ days	+		Positive pressure respiration
3. Postpartum hemorrhage, hysterectomy, peritonitis, <i>hepatorenal syndrome</i> , focal renal cortical necrosis. 27 yr. F	+	+	+	+	Cyanosis	1½ days	+	+	
4. Cholecystectomy, <i>hepatorenal syndrome</i> , pancreatitis, biliary cirrhosis. 71 yr. M	+	+	+	+	Hypermotility, convulsions	2 days	+		
5. Peritonitis following appendectomy, <i>hepatorenal syndrome</i> , unknown. 44 yr. M	+	+	+	+		3 days			Laparotomy
6. Neurosurgical removal of meningioma; <i>cerebral edema</i> . 58 yr. F	+			+	Coma	4 days		+	
7. Exploration of common bile duct; <i>pancreatitis</i> . 58 yr. F	+	+	+	+	Restlessness	4 days			
8. <i>Arsenic poisoning</i> . 31 yr. F	+	+		+	Coma	2 days		+	
9. Exploration of common bile duct; <i>hepatorenal syndrome</i> , peritonitis, pancreatitis. 45 yr. F	+	+	+	+	Coma	3 days			
SUMMARY	9	7	6	9		1½ to 6 days	4	4	

TABLE (continued)
Experience with Artificial Hibernation in Nine Patients

Diagnosis and condition before hibernation. Age, sex	Apparent improvement after onset of hibernation	Life prolonged, days	Reason for failure	Difficulty in hibernation	Sensorium during warming up or at end	During hibernation	
						Diuresis per day	Uremia, mg. %
1. <i>Traumatic pancreatitis</i> , crush syndrome, fractures, uremia. 34 yr. M	++	5 days	Thrombosis and pulmonary embolism	Temperature too low	Good	50 cc.	220-550 mg. %
2. Aortic graft, <i>ischemic necrosis</i> of kidney, uremia. 57 yr. M	++	1½ days	Ischemic necrosis of kidney, pulmonary atelectasis, occlusion of femoral artery	Muscular rigidity, atelectasis	Improved	25 cc.	119-229 mg. %
3. Postpartum hemorrhage, hysterectomy, peritonitis, <i>hepatoarenal syndrome</i> , focal renal cortical necrosis. 27 yr. F	+	?	Overwhelming infection, focal infarct, necrosis of kidneys	Low blood pressure		125 cc.	258 mg. %
4. Cholecystectomy, <i>hepatoarenal syndrome</i> , pancreatitis, biliary cirrhosis. 71 yr. M	+	1	Bronchopneumonia	Respiratory failure	Uncertain	120 cc.	78-180 mg. %
5. Peritonitis following appendectomy, <i>hepatoarenal syndrome</i> , unknown. 44 yr. M	Uncertain	?	Continued fall in blood pressure	Low blood pressure		1200-260 cc.	57 + mg. %
6. Neurosurgical removal of meningioma; <i>cerebral edema</i> . 58 yr. F	++	10 days	Recurrence of spiking temperature after 10 days	None	Improved	Maintained normal	
7. Exploration of common bile duct; <i>pancreatitis</i> . 58 yr. F	++	19 days	Cardiac arrest 3 weeks later, large retropancreatic abscess	None	Good	2000-3100 cc.	24 mg. %
8. <i>Arsenic poisoning</i> . 31 yr. F	+	1 day	Bronchopneumonia	Bleeding from tracheotomy		50 cc.	118 + mg. %
9. Exploration of common bile duct; <i>hepatoarenal syndrome</i> , peritonitis, <i>pancreatitis</i> . 45 yr. F	+	1½ days	Atelectasis	Respiratory difficulty, nosebleed, fall in blood pressure		430-300 cc.	105-165 mg. %
SUMMARY	8	1 to 19 days					

distention becomes less. There are no shivering and goose pimples. The French authors stress the fact that they see no pulmonary complications. We have been less fortunate, but we started out with patients in whom these complications already were present or might be expected.

In a successful hibernation, a state is achieved that differs widely from coma, shock, or narcosis. It is characterized, according to Huguenard, by hypometabolism, hypothermia, hypotension (a systolic pressure that varies from 110 to 90), bradycardia, slow respiration, analgesia, half sleep (better called a state of disinterest), hyposecretion (of saliva, and bronchial, gastric, intestinal, bile, and pancreatic secretions), slowing of the circulation, prolongation of the clotting time, hyperleucocytosis, reduction of azotemia, alkalosis, hypovoltage of the electrocardiogram, and encephalographic waves of normal sleep.

Personal Experiences with Artificial Hibernation in Nine Patients

We have limited our attempts at hibernation to the treatment of patients who, with the currently available methods, but without hibernation, were considered by all concerned as hopelessly ill. The Table gives a summary of our experiences. Some of the patients had very complicated diseases, but the primary diagnoses are summarized as follows: Hepatorenal syndrome, 4; pancreatitis, 2; ischemic necrosis of the kidney, 1; postoperative cerebral edema, 1; and arsenic poisoning, 1.

The main indications for hibernation were the following conditions: high-spiking temperature, 9; uncontrollable deterioration, 9; uncontrollable fall in blood pressure (shock), 7; ileus with marked distention, 6; convulsions, extreme restlessness, and coma, each 2; cyanosis, 1.

In eight patients, apparent temporary improvement occurred after the onset of hibernation. Life was probably prolonged from 1 to 19 days in seven of the nine patients. The sensorium, as far as could be judged during temporary warming up or during the final warming-up period, improved in four of the nine patients.

The difficulties encountered during hibernation were as follows: temperature too low because of "overshooting," 1; muscular rigidity, 1; respiratory failure for unknown reason, 1; bleeding from nose and tracheotomy wounds into the trachea, causing atelectasis, 2; continued fall in blood pressure, 2. The diuresis decreased in five patients, and was maintained in two; in two oliguria had existed prior to hibernation. Azotemia increased in seven patients (up to 550 mg. urea per hundred ml. in one). The following two case reports are presented as examples.

Report of Cases

First case report (Fig. 2, Table). A 34-year-old man was in good health until he was in an automobile accident. He was admitted to a hospital, with a broken leg, a broken

pelvis, broken ribs, and bruises. On the sixth day he developed spiking temperatures. He was transferred to the Cleveland Clinic Hospital on the twelfth day. Extensive bruises and a large hematoma in the right side of the abdomen still were present. He was subicteric. The diaphragm on the right side was paralyzed. He was irrational and restless. His temperature was 40 degrees C. (103 degrees F.). He had uremic frost on his face; the blood urea was 290 mg. per hundred ml. An exact diagnosis could not be made, but it was thought that he might have a crush syndrome. A suspicion of pancreatitis was reinforced by a serum amylase higher than 1000 units.

At first he was treated conservatively. Intravenous infusions of 10 per cent invert sugar, sodium lactate and dextran were given, but the blood pressure fell to 80/60. Hibernation was started on the thirteenth day after the accident (Fig. 2). Dextran, 1 liter, had to be given to sustain the blood pressure around 95/60.

On the third day of hibernation, Cocktail No. 2 was started. On this day, the temperature dropped too low—to 23 degrees C. (73 degrees F.). P waves disappeared from the electrocardiogram; pulse rate was only 30; there was a markedly depressed ST with a negative T (Fig. 3). The temperature gradually came back to 29 degrees C. (85 degrees F.). The patient's color was pink; the electrocardiogram returned to normal (Fig. 3).

On the fifth day of hibernation he was treated with the rotating type of artificial kidney. The blood urea was reduced from 550 to 150 mg. per hundred ml. At times the

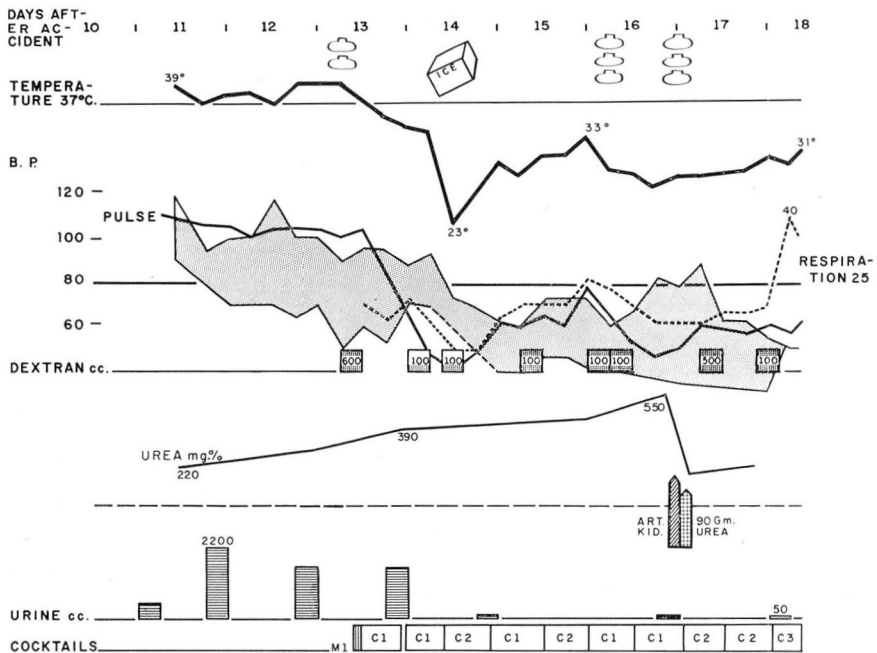


Fig. 2. (First case report, patient No. 1, Table) Hibernation was started where M1 indicates Mélange No. 1. Cocktails No. 1 and No. 2 were alternated. Ice bags and ice block in upper part of graph indicate when ice was applied. During overshooting, temperature went down to 23 degrees C. Dextran was required to keep the blood pressure up, but even then systolic pressure often was less than 80 mm. Hg. The urine volume decreased with the decrease in blood pressure.

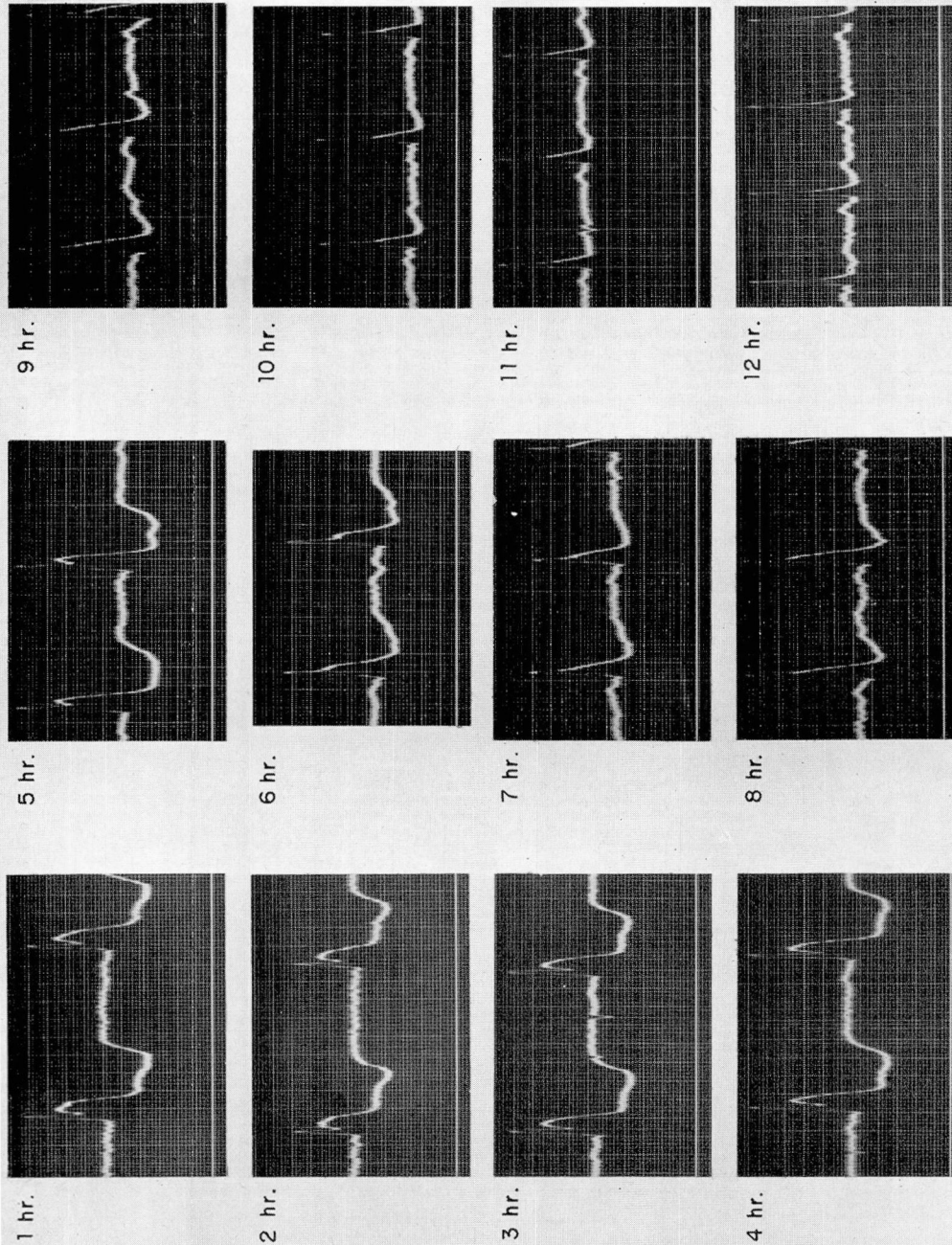


Fig. 3. Electrocardiograms of patient No. 1 during hibernation. Cuts of lead II taken at one-hour intervals. First electrocardiogram taken with body temperature at 23 degrees C. No P waves, broadened QRS, lowering of ST with negative T. While the temperature gradually rose to 29 degrees C., the electrocardiogram returned to normal. (Dr. W. L. Proudfit).

patient was able to answer simple questions. On the sixth day, a rather sudden deterioration of his general condition occurred, with an increase in respiratory rate, cyanosis, and further fall in blood pressure. The patient died that day.

The postmortem examination revealed that multiple small pulmonary emboli were blocking the major part of the branches of the pulmonary arteries. These findings adequately explain the terminal deterioration.

Comment. We believe that this patient's life was prolonged for five days. The lethal complications might have been avoided by the administration of more heparin. We had given only 100 mg. per day because of the many hematomas and bruises present. Diuresis decreased, and the blood urea increased notwithstanding hibernation. Cystoscopy, trephination, treatment with the artificial kidney and a variety of minor procedures were performed without further anesthesia and without difficulty during the period of hibernation.

Second case report (Fig. 4, Table). A 58-year-old woman had recurrent attacks of pain in the right upper quadrant, one of which was associated with a rise in temperature, and she was reported to have been slightly icteric. The gallbladder had been removed 20 years before. The common duct was explored and a cholangiogram was made because the presence of a stone was suspected. No stone was found, and on the third day after

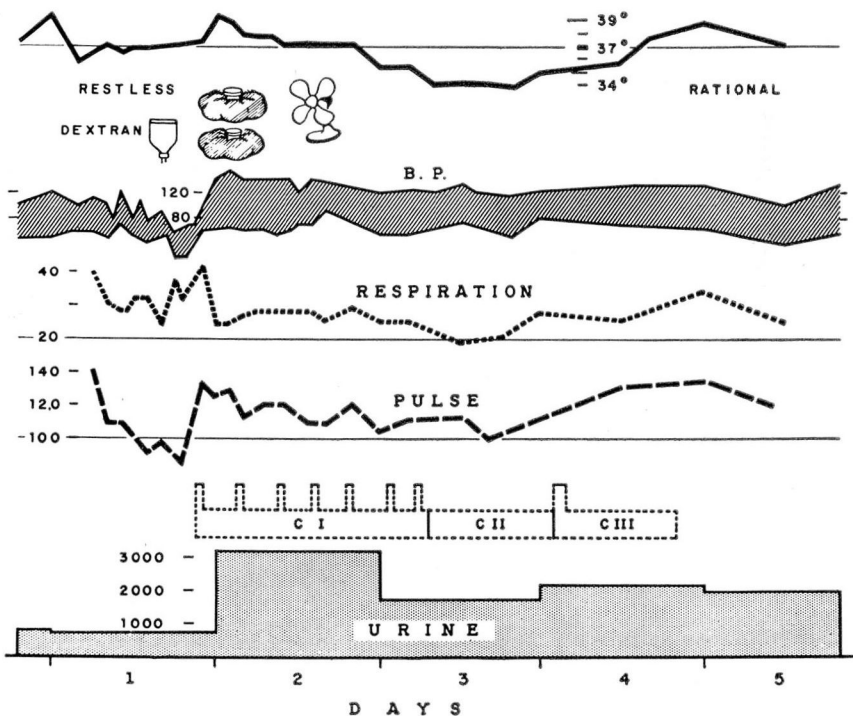


Fig. 4. (Second case report, patient No. 7, Table) Hibernation was started when the blood pressure was 60/40. CI, CII, and CIII indicate Cocktails Nos. 1, 2, and 3. The block-extensions above CI and CIII indicate use of additional Mélange No. 1. The spiking temperatures were controlled and blood pressure was maintained.

operation she developed a fulminating pancreatitis. Heart complications made their appearance, leading to intermittent partial block and at times auricular fibrillation. Her condition continued to deteriorate. She was extremely restless and had to be kept under heavy sedation. There were spiking temperatures up to 40 degrees C. (104 degrees F.), and recurrent falls in blood pressure, the last of which, on the twelfth day after the operation, failed to respond to the usual therapy—including the use of dextran. Her condition evidently was hopelessly deteriorating, and hibernation was started when the blood pressure was 60/40 and she no longer responded to any stimulus. No Demerol hydrochloride was added to the usual Mélange No. 1, as she was comatose already. During the onset of hibernation, the administration of dextran was continued. After a few hours, her blood pressure rose. The temperature increased and more Mélange No. 1 had to be given, this time with Demerol hydrochloride because the patient had awakened. Refrigeration was effected with the help of ice bags and an electric fan. The diagram in Figure 2 shows how Cocktail No. 1 was followed by Cocktails Nos. 2 and 3.

The patient's clinical condition improved from day to day. Cyanosis disappeared. Fluid and electrolyte therapy was continued in order to control losses by gastric and bile drainage. Urine volume increased to three and two liters per 24 hours. Abdominal distention regressed and when she was allowed to warm up on the fourth day, she proved to be clear of mind and cooperative. It seems that a vicious circle had been broken and that the patient then had a chance to recover.

Further convalescence progressed slowly but satisfactorily except for the recurrence of fever. Finally the fever disappeared, but she started to vomit; and one morning, 34 days after the operation and 19 days after the termination of the hibernation, she died suddenly while sitting in a chair.

As the electrocardiogram had continued to show a partial heart block, she probably died from cardiac arrest. At postmortem examination a large retropancreatic abscess was found.

Comment. The convinced hibernotherapist would see it thus: At a time that the body defenses produced spiking temperatures, restlessness, falling blood pressure and cyanosis, further deterioration was arrested by hibernation. The temperature was reduced and controlled; the blood pressure and oxygenation became adequate since cyanosis gave way to pink color. Distention regressed. It seemed that the infection was localized, and sensorium after awakening was clear. Unfortunately, though, the final outcome of the underlying disease was not altered.

Summary and Conclusion

Nine patients, all of whom were considered beyond recovery by more conservative methods, were treated with artificial hibernation. Uncontrollable deterioration, shock, spiking temperature, and restlessness were among the indications for hibernation. The technic of Laborit and Huguenard was followed as closely as possible. In seven patients a rapidly downhill clinical course seemed to be arrested, at least temporarily, and patients who seemed about to die lived 1 to 19 days during or after hibernation. Eight of the nine patients were more comfortable during hibernation. Such signs as spiking temperatures, ileus with distention, convulsions, extreme restlessness, and cyanosis gave way to controlled temperature, less distention, quiescence, and pink color. Two patients recovered

temporarily but finally died from the underlying disease. It is concluded that artificial hibernation deserves further trial in patients with potentially curable disease who presently would succumb to overwhelming aggression or during the struggle to overcome it.

References

1. Laborit, H., Huguenard, P. and others: *Pratique de L'Hibernothérapie en Chirurgie et en Médecine*. Paris: Masson & Cie Editeurs, 1954, pp. 256.
2. Huguenard, P.: Technique et résultats de l'hibernation artificielle; sa place dans la pratique courante. *Anesth. analg.* **1**: 16-53 (Feb.) 1953.
3. Lain, C.: L'hibernation artificielle dans les oblitérations coronarienne et en chirurgie cardio-vasculaire; recherches expérimentales et perspectives cliniques. (Artificial hibernation in coronary obliterations and in cardiovascular surgery: experimental research and clinical perspectives.) *Sem. hôp. Paris* **29**: 4171-4174 (Dec. 26) 1953.
4. Chippaux, C.: Application of artificial hibernation to war surgery in Indochina. *International Record of Medicine and General Practice Clinics* **167**: 328-332 (June) 1954.
5. Jaulmes, C.: Artificial hibernation; experimental studies. Paris (Translated manuscript received from Dr. E. I. Evans, Medical College of Virginia, Richmond, Virginia).
6. de Lavergne, V. and Schmitt, J.: Artificial hibernation in scarlet fever. In *Foreign Letters*, *J.A.M.A.* **153**: 1196-1197 (Nov. 28) 1953.
7. Osborn, J. J.: Experimental hypothermia: respiratory and blood pH changes in relation to cardiac function. *Am. J. Physiol.* **175**: 389-398 (Dec.) 1953.
8. Swan, H., Zeavin, I., Blount, S. G., Jr. and Virtue, R. W.: Surgery by direct vision in the open heart during hypothermia. *J.A.M.A.* **153**: 1081-1085 (Nov. 21) 1953.