

THE ELECTROENCEPHALOGRAM IN HYPOTHERMIA WITH CIRCULATORY ARREST

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IN RECENT years, the use of the electroencephalograph as a monitoring device during anesthesia has increased. Hale and Moraca¹ and Scott² mentioned changes seen in the electroencephalogram of patients subjected to hypothermia and others have studied the electroencephalogram in hypothermic animals.^{3, 4, 5} Similar studies during circulatory occlusion in animals have also been reported.^{3, 6, 7, 8} The purpose of this communication is to present the results of electroencephalographic monitoring of patients undergoing hypothermia and cardiac surgery with total circulatory occlusion.

METHOD

Electroencephalographic tracings were made during the course of hypothermia and cardiac surgery in 108 patients. After the induction of anesthesia, midline fronto-occipital needle electrodes were placed in the scalp, and recordings were made intermittently with a Grass model III D electroencephalograph as hypothermia and surgery progressed. Thiopental or thiopental and cyclopropane were usually used for induction of anesthesia. Maintenance of anesthesia prior to hypothermia was with oxygen, ether, and tubocurarine chloride, except that cyclopropane was used in one case and nitrous oxide supplemented with thiopental in three. Hypothermia was induced by body immersion in cold water. Temperature was monitored by rectal and/or esophageal thermometers. During hypothermia the patients' lungs were artificially ventilated with oxygen, and muscular relaxation was maintained with curare. Infrequently an additional anesthetic agent, usually nitrous oxide, was needed after hypothermia had been established; therefore, there was a progressive reduction of chemical anesthesia as the anesthetic effects of hypo-

thermia developed. No direct measurements of chemical anesthetic concentrations were made. We believe that chemical anesthesia was minimal, and in most cases negligible, at temperatures below 33 C. Subsequently the electroencephalographic records were visually analyzed to determine frequency and voltage. Not all 108 records were complete or free from electrical artifacts; each record adequate in the parameter considered was used in computing the average values reported herein.

Animal experiments were conducted with 12 mongrel dogs. The animals were anesthetized with intravenous pentobarbital, their tracheas were intubated and their lungs were artificially ventilated with oxygen. Blood pressure was monitored from the femoral artery by a Statham transducer coupled to a cathode ray oscilloscope. Cooling was accomplished by body immersion in ice water. Temperature was recorded with a rectal thermometer. The electroencephalographic recordings were made from fronto-central needle electrodes on a Grass recorder, and were visually analyzed.

RESULTS

First, the electroencephalographic effects of the cooling process itself in patients and in animals will be described. Second, the electroencephalographic changes seen in patients during and following circulatory occlusion will be presented.

RESULTS DURING COOLING: *Patients.* The electroencephalographic changes occurring while 74 human patients were being cooled are summarized in table 1. Beginning temperatures were 36 to 37 C. and changes were determined at the lowest temperature reached. Some subjects showed more than one effect, such as decreased frequency associated with increased voltage. Twenty nine patients showed no change as cooling progressed (table 1). Thirty-nine patients showed a tendency toward slowing of frequency, even though this

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TABLE 1
ELECTROENCEPHALOGRAPHIC CHANGES IN 74 PATIENTS DURING HYPOTHERMIA

Number patients	No Change	Decrease in Frequency			Decrease Voltage	Increase Frequency	Increase Voltage
		Less than 25%	25%-50%	Greater than 50%			
	29	25	9	5	4	5	12

slowing was usually slight. A typical change was a reduction from 16-17 cycles per second at 36 C. to 13-14 cycles per second at 30 C. Figure 1 presents a typical progression of changes as temperature was lowered. Five records of patients whose temperatures fell below 29 C. were satisfactory for analysis. Figure 2 shows the changes in frequency seen in these records. With one exception there was a decrease in frequency. In two voltage increased, in two others no change in voltage appeared. The one record showing increased frequency also showed a decreased voltage.

During rewarming by diathermy, muscle artifact and electrical interference made the records largely illegible, so no recovery data can be reported.

Dogs. Little change was seen in most of the dogs' electroencephalograms until temperatures were reached below those usual for clinical hypothermia.

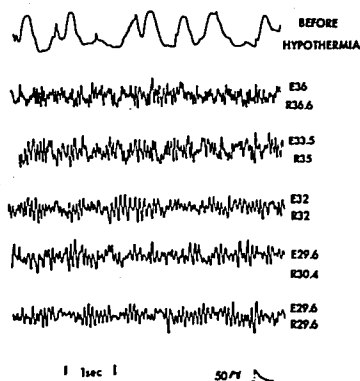


FIG. 1. Typical segments of the electroencephalogram as hypothermia was induced. E = esophageal, R = rectal temperature in degrees C.

Below 28 C. most animals showed a progressive reduction in voltage and concomitant slowing of frequency until the tracing became flat (fig. 3). Blood pressures diminished as cooling progressed and often fell most precipitously at the time that the electroencephalogram showed the most dra-

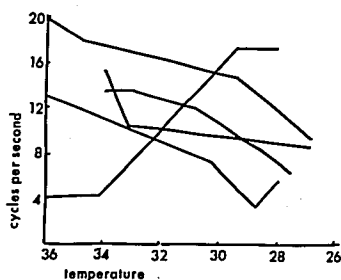


FIG. 2. The frequency changes seen in each of 5 patients as hypothermia below 29 C. was induced.

matic change. Figure 4 illustrates the relationship of blood pressure to the point at which the electroencephalogram became flat. One animal exhibited a rise in blood pressure from 110/80 mm. of mercury to 160/50 mm. of mercury at the time the electroencephalogram became flat. This causes one to suspect that the decline of cerebral activity was not a result of a decline of blood pressure. Rather, the blood pressure drop and slowing of cerebral activity were concomitant changes resulting from hypothermia.

Figure 3 shows a peculiar low voltage, fast frequency activity well established at 28 degrees. This activity, as will be discussed, is not distinguishable from that seen after circulatory occlusion in man. Eight animals

showed this type of activity. Three of these showed progressive reduction in amplitude of this fast activity until it was no longer discernible and the record became isoelectric (flat).

RESULTS AFTER CIRCULATORY OCCLUSION: After circulation in man was completely stopped by ligatures around the venae cavae and aorta, most patients showed a regular sequence of electroencephalographic changes (fig. 5). Initially there was a latent period in which no discernible change in frequency or voltage appeared. The mean duration of this latency was 15 seconds. After this latent period there was an interval of 13 seconds

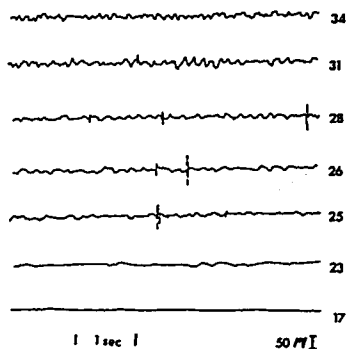


FIG. 3. Portions of the electroencephalogram of a dog during induction of deep hypothermia. Temperature shown at the right of the figure is in degrees C.

average duration of progressive slowing of frequency, usually associated with an increased voltage. As the frequency slowed to 1-3 cycles per second, there usually appeared superimposed activity which was of less than 10 microvolts amplitude with an irregular fast (greater than 20 cycles per second) frequency. This was descriptively termed low voltage background fast activity, and occurred an average of 28 seconds after occlusion. It persisted after other frequencies had disappeared, and it disappeared in an average of 30 seconds following which the tracing became isoelectric for the duration of occlusion. Some deflections of the writer pen occurred from

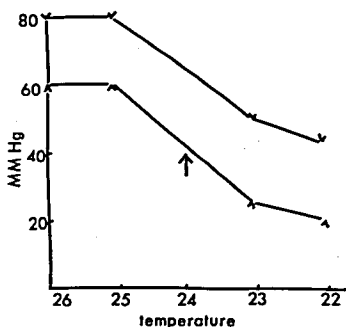


FIG. 4. Blood pressure of a representative animal. Arrow shows beginning of isoelectric Electroencephalogram in this animal. Temperature in degrees C.

time to time but we believed that these represented movement artifact. In summary, after occlusion there was a latent period, a period of progressive slowing of frequency, a period of low voltage fast frequency activity, and an isoelectric period in which no activity was detectable. The mean times of the onset of each of these periods measured from the time of occlusion are summarized in table 2. The latent period is represented by the interval between occlusion and the onset of slowing.

Body temperature exerted some effect on the period of electrical activity after occlusion. Table 3 shows the results of circulatory occlusion in patients with temperatures above and below 29 C. Electrical activity tended to persist longer after occlusion in the lower temperature range. The periods from occlusion to low-voltage-background-fast activity, and from

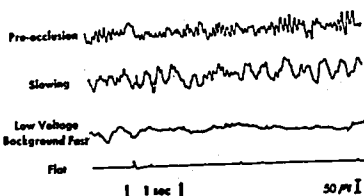


FIG. 5. Representative changes in the electroencephalogram after circulatory occlusion during hypothermia.

TABLE 2

AVERAGE TIME (AND STANDARD DEVIATION) FOR APPEARANCE OF ELECTROENCEPHALOGRAPHIC CHANGES AFTER CIRCULATORY OCCLUSION IN MAN

Slowing	Low Voltage Fast	Isoelectric (Flat)
14.7 sec. S.D. 8.4	27.6 sec. S.D. 17.8	57.6 sec. S.D. 34.9

occlusion to flat electroencephalogram, above and below 29 C., were statistically different ($p < 0.05$ in each case).

Upon release of occlusion so that blood again flowed to the brain, there was a less regular sequence of events. Initially there was a latent period in which the previous isoelectric line continued. When activity began to appear, it was variable, sometimes occurring as low-voltage-background-fast activity, other times as a return of a fast, a medium, or a slow frequency activity. The electrical activity steadily changed until the preocclusion, normal activity was present. The rate at which such activity returned was related to duration of occlusion (fig. 6). There was a definite delay in return of cerebral activity with longer occlusion times. Some patients did not return to preocclusion "normal" activity during the time of observation, and therefore could not be included in the calculation of the recovery times of figure 6. Had these patients all been followed until return to normal, the average recovery times would have been longer.

Time required for recovery of cerebral activity at temperatures below 29 C. was shorter than that above 29 C. The return to normal,

TABLE 3

TIMES FROM CIRCULATORY OCCLUSION TO THE ELECTROENCEPHALOGRAPHIC CHANGES AT TEMPERATURES ABOVE AND BELOW 29 C. (AVERAGE TIMES AND STANDARD DEVIATIONS)

	Slowing	Low Voltage Fast	Isoelectric (Flat)
Above 29 C.	14.9 sec. S.D. 9.7	27.1 sec. S.D. 12	56.6 sec. S.D. 32.8
Below 29 C.	14.5 sec. S.D. 7.7	42.2 sec. S.D. 27.9	80.8 sec. S.D. 54.5

at temperatures below 29 C., required a mean of 8.5 minutes, while the mean for those above 29° was 17 minutes ($p < 0.05$). The time from release of occlusion to first activity in cases below 29 C. was also shorter than in those above 29°, but this difference was not statistically significant.

The electroencephalograms prior to occlusion were graded as either "good," "fair," or "poor" on the basis of the frequencies in the tracing. Those graded "good" had no frequencies slower than the alpha (8-12 cycles per second) range. Those graded "fair" had frequencies of 4-7 cycles per second, and those graded "poor" had frequencies slower than 4 per second. Other activity may have been superimposed, but the presence of slow activity was considered sufficient to evaluate the tracing as either "fair" or "poor." In only one measured parameter did the condition of the preocclusion encephalogram appear to influ-

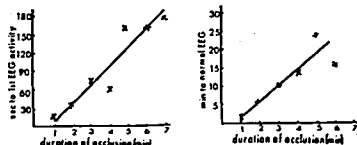


FIG. 6. Relationship of duration of circulatory occlusion to return of EEG activity.

ence results. Those graded "poor" were found to show a statistically significant prolongation of the time from release of occlusion to return of normal (preocclusion) activity. The mean of all cases combined was 17 minutes, while the mean of those graded "poor" was 49 minutes ($p < 0.05$).

The relation of the electroencephalogram to patient mortality was considered. Prolonged return to a normal electroencephalogram after occlusion was found to be of prognostic importance. In eight patients there was no return to preocclusion activity within two hours after release of occlusion. Of these, three died, a mortality rate of 37.5 per cent. The other five recovered adequately. In the entire series there were six deaths, a mortality rate of 5.5 per cent. No other prognostic implications of the electroencephalogram were found.

A brief discussion of each of the six deaths

will be presented: The first had multiple episodes of ventricular fibrillation after seven minutes of occlusion. The electroencephalogram in this case showed only electrocardiographic artifact. Postoperatively there was no return of consciousness. The patient died of hemorrhagic diathesis one and one-half days postoperatively. The second patient had his circulation occluded ten minutes. Electroencephalographic activity returned in two minutes but did not recover beyond 4-6 cycles per second during observation. This patient died on the first postoperative day secondary to bleeding diathesis. The third patient died on the fifth postoperative day of pulmonary edema and heart failure. This patient had not recovered normal electroencephalographic function in two hours following release of occlusion.

The remaining three fatal cases showed electroencephalographic recovery to preocclusion levels. One patient died two days after operation of bilateral internal jugular vein thrombosis. Another had a total of seven circulatory occlusions and died on the third postoperative day subsequent to bleeding. The third patient showed good immediate postoperative recovery but died in congestive heart failure thirty-six hours postoperatively.

DISCUSSION

Several reports have discussed the electroencephalographic changes in man during hypothermia. Hale and Moraca¹ reported slowing of frequency and decrease in voltage in the electroencephalogram with cooling. Their patients were cooled by infusion of cold blood from a pump oxygenator. Scott's² report concerned twenty-five patients cooled to 28 C. for resection of berry aneurisms. With decrease in temperature there was a reduction in voltage from 60-80 microvolts to 50 microvolts. Below 30 C. the voltage drop continued and the record became irregular but without suppression. No beta (fast) activity was seen but alpha frequencies sometimes persisted.

More extensive work has been reported in animals. McMurrey, Bernhard, Taren and Bering³ described changes seen in the electroencephalogram of monkeys subjected to hypothermia and cerebral occlusion. They found changes similar to those seen after increasing

doses of pentobarbital. They also observed flattening of the electroencephalogram after one minute of total occlusion, and noted recovery time was directly related to occlusion time. Callaghan, McQueen, Scott and Bigelow,⁴ also working in monkeys, reported progressive flattening of the electroencephalogram as temperature was lowered. At 20 C. there was minimal activity present. During rewarming the rhythms returned in reverse order. Gaenshirt, Krenkel and Zylka⁵ cooled isolated cat's heads by perfusing with cooled blood from a donor cat, and found a slowing of frequency with an increase in voltage to 30 C.; below 30 C. dysrhythmia appeared with slow frequencies dominating and the voltage decreased. Their records became isoelectric between 15 and 20 C.

Hirsch and his associates^{6,7,8} reported on the electroencephalogram in cats during circulatory occlusion. After occlusion, cerebral activity continued for a period which they termed the survival time (*erholungszeit*). At normothermia this time averaged 20 to 25 seconds. At normal temperatures the recovery latency (*erholungslatenz*) was 30 seconds after one minute occlusion, and 35 to 120 seconds after a 10 minute occlusion.

Our observations in man reveal a slowing of frequency and agree generally with the above mentioned situations in which the subjects were animals. We did not find slowing as extensive as that which Hale and Moraca reported. Perhaps some factor in the method of cooling accounts for the difference. Animal studies indicate that if temperatures are low enough hypothermia itself can cause a complete cessation of cerebral electrical activity, but we have not utilized such low temperatures in man.

The effects of sudden complete cerebral ischemia on the electroencephalogram of man were characteristic and followed a similar pattern from patient to patient. The lower temperatures appeared to increase the resistance of the brain to this ischemia. However, at all temperatures used in this series, complete flattening of the electroencephalogram occurred after circulatory arrest.

The return of cerebral electrical activity was related to duration of occlusion. The shorter the occlusion, the more rapid the return. It is

our impression that excessively delayed return of activity after occlusion may have resulted from inadequate postocclusion circulation. For example, patients whose hearts fibrillated uniformly demonstrated a delay in return to normal activity. Slow return to normal activity was related to postoperative mortality, possibly the result of cerebral damage, in which case the damage produced the slow electroencephalographic picture. On the other hand, the "poor" electroencephalogram may have been a result of circulatory insufficiency which subsequently became the major factor in mortality. Our experience favors poor circulation rather than brain damage as the cause of death.

Although three patients, whose normal electrical activity failed to return in two hours, died, it should be noted that 5 of 8 patients in this category survived. Therefore, while the prognosis in this situation is relatively poor, it is by no means hopeless.

The low-voltage-fast-frequency activity seen both on occlusion and return of circulation is an interesting phenomenon. It appears to be similar to the "file pattern" reported previously by others.⁹ This low-voltage-fast-frequency "file" activity is said to carry grave prognosis when seen in patients after acute cerebral anoxia,⁹ yet this activity usually appears in patients having elective circulatory occlusion under hypothermia. Following occlusion of circulation this activity is the last to disappear before the electroencephalogram becomes isoelectric, and is frequently the first to reappear after circulation has been resumed. In many cases this low-voltage-fast-frequency activity can be followed for seconds to minutes, then it gradually increases in amplitude until it becomes readily discernible beta (greater than 15 cycles per second) activity. Figure 7 presents a typical sequence of events after resumption of circulation in man showing the gradual increase in amplitude of this activity until it reached a level of greater than 10 microvolts. At this amplitude it became discernible as beta frequency activity, and usually increased further in voltage until it reached preocclusion levels. One might presume, therefore, that this low voltage phase is merely the first part (or last part, depending on circumstances) of good cerebral activity. The appearance of similar electrical activity during profound hypo-

thermia in animals is further evidence of the nature of the cerebral activity. As shown in figure 3, this pattern was the last evidence of cerebral activity before the electroencephalogram became isoelectric.

SUMMARY

A study of the electroencephalograms of 108 human beings subjected to hypothermia by total body cooling has been reported. There was often a negligible change. In one-half of the patients, there was a tendency toward slowing of frequency usually not greater than twenty-five per cent. Twelve dogs cooled to below 28 C. developed isoelectric (flat) electroencephalograms.

After occlusion of circulation for cardiac surgery there was a short latent period in which no electroencephalographic change occurred, then the frequency progressively slowed. A superimposed low voltage fast frequency activity developed and persisted after cessation of the slower frequencies. The electroencephalogram then became isoelectric and except for artifacts, remained isoelectric for the duration of the occlusion. After release of the occlusion and resumption of circulation, cerebral activity reappeared and progressively returned to the preocclusion level. Failure of the electroencephalogram to return to the preocclusion condition was a serious prognostic sign.

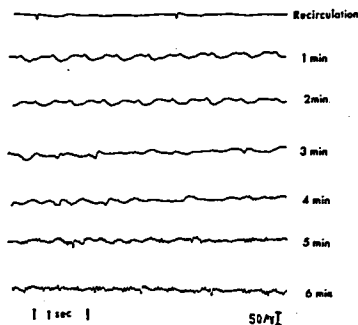


FIG. 7. Segments illustrating the gradual development of beta activity from low voltage background fast ("file") activity in man.

Low voltage fast frequency activity, similar to the "file pattern" reported by others, was regularly seen after circulatory occlusion and during recovery from circulatory occlusion. Its significance is discussed.

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