Neurological syndromes after cardiac arrest.

J J Caronna and S Finklestein

Stroke. 1978;9:517-520
doi: 10.1161/01.STR.9.5.517
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

Current Concepts of Cerebrovascular Disease — Stroke

Neurological Syndromes After Cardiac Arrest

JOHN J. CARONNA, M.D. AND SETH FINKLESTEIN, M.D.

CARDIOPULMONARY resuscitation has become commonplace activity, not just in emergency rooms and hospital intensive care units but even on the street. Largely because of the efforts of paramedical personnel in the community and the education of laymen in the techniques of cardiopulmonary resuscitation, there are more survivors from cardiac arrest than ever before. Neurological outcomes among survivors cover a broad spectrum, ranging from complete recovery to the vegetative state. Patients who awake promptly after resuscitation provide a gratifying experience to their physicians and present no problem in prognosis. However, neurologists are often asked to see patients in coma following cardiac arrest to help predict the degree of eventual recovery and to advise the family and plan future therapy.

From our experience at San Francisco General Hospital we shall address two questions commonly posed by physicians caring for postcardiac arrest patients: What deficit and recovery profiles may be expected in patients after cardiac arrest? Can eventual neurological outcome be predicted for the individual patient?

Neurological Outcomes After Cardiac Arrest

Cardiac arrest may be thought of as causing both "metabolic" and "structural" damage to the central nervous system. Patients with brief episodes of systemic circulatory arrest who suffer milder degrees of cerebral anoxia-ischemia demonstrate the clinical features of a reversible "metabolic encephalopathy." Coma, if present, lasts only a few hours (12 at most). On awakening, these patients demonstrate few "focal" motor, sensory, or intellectual deficits but may be transiently confused or amnestic for hours to days. Recovery is rapid and complete, so that these patients usually can resume their previous occupations (Good Recovery).

By contrast, patients with more severe systemic anoxia-ischemia suffer structural damage to specific areas of the brain as if they had had a stroke. The vulnerable areas of the nervous system include the cerebral cortex, hippocampi, the cerebellum, the basal ganglia, and sometimes the spinal cord. Patients in this group are usually in coma for at least 12 hours and on awakening manifest lasting focal or multifocal motor, sensory, and intellectual deficits. Recovery is often incomplete and slow, on the order of weeks to months. Some of these patients are able in time to lead an independent existence at home despite residual neurological deficits (Moderate Disability), while others, severely disabled and dependent, remain in nursing homes (Severe Disability). Others with more widespread destruction of brain may remain hospitalized in a state of wakefulness without awareness (Vegetative State) or die a neurological death (Brain Death).

The following prototypical case histories illustrate the spectrum of neurological disability after cardiac arrest.

Case 1 — Transient Amnesia Followed by Complete Neurological Recovery

A 26-year-old woman with Wolff-Parkinson-White syndrome was brought by ambulance to San Francisco General Hospital after a cardiac arrest at home. Within 12 hours she responded appropriately to verbal commands. At 24 hours she was noted to be "confused." Neurological examination was normal except for her mental status. The patient was alert, euphoric, and had no insight into her condition. She knew the year but not the month and named the hospital incorrectly. She stated that she had just arrived by car for a "checkup." She had immediate recall of digits and objects but could not remember 3 objects or the name of the hospital after 2 minutes. Remote memory of personal events was preserved except that she gave her one-year-old son's age as "9 months." She could not remember the President's name nor select it from among several choices. Her ability to use language, calculate, interpret proverbs, and detect similarities and differences was intact. An electroencephalogram was normal. By the fourth day after cardiac arrest, the patient's memory began to improve; she appeared concerned and incessantly asked for details of her resuscitation. One month later, her anterograde and retrograde memory was normal except for a "blank period" of several days.

Comment. We have followed 10 such patients with an amnestic syndrome as their only neurological disability after cardiac arrest. The pattern of memory loss is severe anterograde and variable retrograde

Reprinted from *Current Concepts of Cerebrovascular Disease — Stroke*, May-June, 1978, edited by Arthur G. Waltz, M.D., published and copyrighted by The American Heart Association.

Dr. Caronna is Chief of Neurological Services, San Francisco General Hospital, San Francisco, CA. Dr. Finklestein is Resident in Neurology, University of California, San Francisco.

Reprints may be obtained from affiliates of The American Heart Association.

TABLE 1 *Postcardiac Arrest: Prototypical Neurological Syndromes*

A.	No structural damage (coma < 12 hours) Complete recovery; transient amnesia
B.	Focal or multifocal structural damage (coma > 12 hours) Cortex: Amnesia; dementia Bibrachial paresis; quadriparesis Cortical blindness; visual agnosia Spinal Cord—paraparesis Other—Ataxia, seizures, myoclonus, extrapyramidal signs
C.	Global (no recovery of consciousness) Cortex—vegetative state; neocortical death Cortex + brainstem (± spinal cord)—brain death

amnesia with preservation of immediate and remote memory, resembling that of Korsakoff's psychosis. All patients showed a bland and unconcerned effect and confabulated while amnestic. In 6 patients recovery was complete within 7 to 10 days; in 4, amnesia persisted for a month or longer. (The length of time required for recovery (days) and the occasional instances of incomplete recovery distinguish this syndrome from transient global amnesia and the postictal state. We suspect that transient postcardiac arrest amnesia is not uncommon and may represent reversible bilateral ischemic damage to the hippocampi.[1]

Case 2 — Focal Structural Damage (Cortical Blindness) with Late Recovery

A 64-year-old Chinese-speaking woman with ischemic heart disease collapsed in the street and was brought to the hospital. Multiple electroshocks were required to convert ventricular fibrillation to normal sinus rhythm. At 12 hours after resuscitation, she remained comatose. Noxious stimulation produced stereotyped flexion of both arms (decorticate posture) without eye opening. There were spontaneous roving eye movements, intact pupillary and corneal reflexes, full oculocephalic responses (doll's eyes), brisk tendon reflexes, and bilateral extensor plantar responses. By 24 hours the patient opened her eyes and purposively withdrew arms and legs. By 1 week she appeared fully conscious. However, her speech was confused, and she did not follow commands given in Chinese. At this time it was noted that she failed to blink to visual threats or to follow a moving object. Over the course of 1 month, her speech and mental status returned to normal, according to her family, and she became ambulatory with assistance. She could not locate or name simple objects held before her eyes but could name the same objects when they were placed in either hand. By 6 weeks after cardiac arrest, the patient could follow objects and count fingers but still had difficulty identifying objects by visual clues alone. Computed tomographic and radionuclide brain scans were normal. Visual evoked responses suggested abnormal cortical responses bilaterally. The patient was discharged home. Examination of the visual system at 3 months was normal.

Comment. Partial or complete cortical blindness, an uncommonly recognized sequel of systemic circulatory arrest, usually is transient but rarely may be permanent.[2] In the present case cortical blindness probably resulted from disproportionate ischemia of both occipital poles occasioned by their location in an arterial border zone. Under certain circumstances transient circulatory arrest will lead to focal infarctions concentrated in the border zones between the areas supplied by the major cerebral arteries. These border zones occur in the cerebral cortex, cerebellum, basal ganglia, and spinal cord. In the cerebral cortex ischemic necrosis occurs most commonly and is most severe in the parieto-occipital regions where the territories of the anterior, middle, and posterior cerebral arteries meet. Necrosis usually decreases toward the frontal and temporal poles along the anterior-middle and middle-posterior cerebral arterial boundary zones, respectively.[1]

Bilateral infarction in the border zone between the anterior and middle cerebral arteries is responsible for the bibrachial paresis, sparing the face and legs which is often seen after cardiac arrest.

Case 3 — Focal Structural Damage to the Spinal Cord Without Cerebral Infarction

A 50-year-old man collapsed while jogging. Cardioversion was successful, and within minutes he was alert and moved both arms appropriately to verbal commands. He was admitted to intensive care for cardiogenic shock, aspiration pneumonia, and renal failure. Two days later, the patient was noted to have painless, flaccid loss of motor function including sphincter control below a mid-thoracic level. Deep tendon reflexes were brisk in both arms but absent in the legs. There were no plantar responses. Sensation to pinprick and temperature was absent, and appreciation of light touch, deep pain, and vibration was reduced below a mid-thoracic level. Position sense was absent in the feet but present to gross movements at the knees and hips. Thoracic spine films were negative. The following day a peritoneal catheter placed for dialysis returned fecal-stained fluid. Emergency laparotomy revealed infarction of the small and large bowel. The patient died on the fourth hospital day.

Pertinent findings at autopsy included no evidence of dissection of the aorta or occlusion of any of its branches to the bowel or spinal cord. There was softening of the spinal cord below the mid-thoracic region. On microscopic examination there were degenerative changes in the anterior horn cells throughout the lower thoracic and lumbar regions. The brain was normal.

Comment. The spinal cord generally is considered to be more resistant to transient ischemia than the brain. The present case of isolated spinal cord infarction emphasizes that complete necrosis of the central structures of the spinal cord can occur in critical border zones at the periphery of the territory supplied by a main contributory vessel. These border or "watershed zones" occur in the upper and lower

thoracic and lumbar regions and are not only at risk from occlusion of one of these arteries but also from any profound drop in perfusion pressure. The syndrome of spinal stroke due to hypotension has been described in 11 patients by Silver and Buxton.[3] All had flaccid paralysis of the lower limbs and urinary retention. Ten patients had an upper sensory level in the thoracic region; in all cases pain and temperature were more affected than light touch or position sense.

The present case is also notable for the presence of bowel infarction associated with nonocclusive intestinal ischemia. Ischemic colitis has occurred in elderly patients with organic heart disease and in healthy young adults, in each case precipitated by a hypotensive episode. Nonocclusive intestinal ischemia should be considered in patients who complain of abdominal pain after a hypotensive episode.

Case 4 — Global Destruction of the Cerebral Cortex with Electrocerebral Silence but Preserved Brainstem Function (Neocortical Death[4])

A 55-year-old man with a history of chronic alcoholism and untreated seizures was brought to the hospital after a seizure. While waiting in the emergency ward he suffered a cardiorespiratory arrest. Following resuscitation he continued to have seizures which were controlled with parenteral phenytoin. Neurological examination at 12 hours revealed no response to noxious stimulation; the limbs were flaccid with preserved tendon reflexes. All brainstem reflexes were intact except for absent doll's eyes and dysconjugate ice-water caloric responses. The latter findings were transient and probably due to phenytoin. On day 5 after arrest, the patient opened his eyes but was otherwise unchanged. During the second week after resuscitation, the patient displayed roving conjugate eye movements. Electroencephalograms on the fifth, tenth, and thirtieth hospital days were isoelectric at maximal gain. The patient died of respiratory failure 5 weeks after admission.

At autopsy there was generalized cortical atrophy. The brownish-yellow cortical residue was separated from the white matter by a band of laminar necrosis. Microscopically, necrosis was generalized within the cortex, subcortical grey matter, and cerebellum and involved parts of the brainstem caudally as far as the pons.

Comment. Patients with cardiac arrest and severe irreversible brain damage rarely survive for more than a few days. In the case reported here, unconsciousness with an isoelectric EEG persisted for 5 weeks after cardiac arrest. Eye opening, sleep-awake cycles, spontaneous roving horizontal eye movements, and other reflex activities at brainstem and spinal cord levels were present, but the patient remained in a functionally decorticate state of wakefulness without awareness (persistent vegetative state or akinetic mutism). Detailed neuropathological analysis indicated that the neocortex had been destroyed while certain brainstem and spinal structures remained intact. This neuropathological condition has been termed neocortical death[4] and must be distinguished from total cerebral and brainstem destruction (brain death).

TABLE 2 *Correlation Between Clinical Signs and Levels of Brain Function*

Anatomical region	Neurological sign
Cerebral hemispheres	Verbal responses Purposive movements
Brainstem	Reflex motor movements: Decortication Decerebration
Reticular activating system	Eye opening
Midbrain CN III	Reactive pupils
Pons CN V + VII CN VIII, VI, III + MLF	 Corneal reflex Doll's eyes and ice water responses
Medulla	Breathing Blood pressure
Spinal cord	Deep tendon reflexes

Prognostic Features of Postcardiac Arrest Coma

The criteria for predicting neurological outcome after cardiac arrest are far from certain. In order to define more accurately those features, clinical or laboratory, which predict outcome, a prospective study of cardiac arrest cases was begun at San Francisco General Hospital in December, 1975 and is still in progress.[5]

Patients entered in the study were resuscitated by standard means. All were in coma 12 hours after resuscitation and survived for at least 24 hours. Patients were considered "comatose" who 1) did not open their eyes either spontaneously or to any stimulus, 2) uttered no sounds or comprehensible words, and 3) did not follow commands or move their extremities purposively to localize or resist noxious stimuli.[6]

Clinical testing involved standard tests of motor, sensory, and brainstem function.[6] Particular attention was paid to eye opening, spontaneous and reflex eye movements, speech, and the motor response to commands or to noxious stimuli applied separately to the arms, legs, and face. These clinical signs have specific anatomical correlates (table 2).

To date 50 patients have been followed (table 3), and 5 outcome groups have been identified, based on clinical examinations at 1 month after arrest: good

TABLE 3 *Patients in Coma After Arrest*

Men = 32
Women = 18
Mean age = 62 (22–83) years
Myocardial infarct = 29 (58%)
Ventricular fibrillation or asystole = 48 (96%)
Arrest out of hospital = 38 (76%)

TABLE 4 *Outcome of Coma After Cardiac Arrest*

	GR*	MD	SD	PVS	D
Men	2	2	4	3	21
Women	4	2	1	2	9
Total	6	4	5	5	30

*See text for abbreviations.

recovery, moderate disability, severe disability, persistent vegetative state, and death (table 4). In patients who recovered consciousness but died later, the best neurological performance attained any time within 1 month of the onset of coma was taken as the result.

Certain features were not of predictive significance. There was no difference in age among patients in the 5 outcome groups. Lumbar puncture and radionuclide and computed tomographic brain scans also were not helpful. The conventional EEG, in general, merely confirmed the clinical impression derived from physical signs.

Univariate analysis identified clinical signs that were significantly different among the outcome groups. Certain signs indicative of impaired brainstem function were unfavorable (table 5). At 12 and 24 hours after resuscitation, the absence of pupillary responses, corneal reflexes, or deep tendon reflexes implied death or vegetative state. Absent doll's eyes or calorics reliably predicted death or vegetative state in patients not given ophthalmoplegic agents, e.g., phenytoin. At 12 hours flexor (decorticate) or extensor (decerebrate) posturing did not help predict outcome, but at 24 hours or longer persistence of either response heralded death, vegetative state, or severe disability.

Certain signs indicated a favorable prognosis (table 5). Spontaneous roving horizontal eye movements was a good sign at 12 to 24 hours but thereafter occurred in patients in all outcome groups. Purposive movement of face, arms, or legs was a good sign at any time after arrest, and the pattern of such movements distinguished patients with a good recovery or moderate disability from those with severe disability (quadriparesis). Speech and comprehension were good signs in the first 48 hours and identified patients with a good to moderate prognosis.

The value of precise, repeated clinical observations during the first 48 hours after cardiac arrest is borne out in this study by the association of different signs with favorable and unfavorable neurological outcomes. In particular, signs reflecting the return of cortical activity implied survival.

The principle that limited hypotension may produce limited or focal cerebral dysfunction with specific neurological findings forms the basis for the clinical examination that we have used. Border zone infarcts may account for the disproportionately paretic arms compared to legs, or arms and legs compared to face, that we have observed in some patients recovering from cardiac arrest. It is for this reason that we recommend an individual assessment of the arms, legs, and face for evidence of purposive behavior.

TABLE 5 *Predictive Clinical Signs*

	12 hr	24 hr	48 hr
Unfavorable			
Pupils (no reaction)	×	×	—
Corneals (absent)	×	×	—
Calorics (absent)	×	×	—
Deep tendon reflexes (absent)	×	—	—
Decerebration	—	×	×
Decortication	—	×	×
Favorable			
Spontaneous roving eye movements	×	×	—
Purposive withdrawal	×	×	×
Speech	—	×	×
Follow commands	—	×	×

This study sought to identify clinical signs that might be used to predict outcome in cases of post-arrest coma. Clinical signs have been emphasized because they are simple and readily elicited without the need for elaborate equipment. Others have noted that there is a correlation between outcome and clinical features, but previous attempts to devise a reliable prognostic system have been unsuccessful because of overemphasis on single indicators or on signs elicited only once, usually on admission.

At present, the number of cases is too small and the duration of follow up too short for a confident prediction of outcome in every case, but the predictive powers of clinical signs may be improved by analysis of additional cases still being collected. Further studies are planned to correlate clinical signs with electrophysiological investigations such as cortical and brainstem evoked potentials. The trends which have emerged from this study suggest that repeated clinical observations in coma after cardiac arrest will permit neurological outcome to be predicted with a high degree of probability.

References

1. Brierley JB: Pathology of cerebral ischemia. *In* McDowell FH, Brennan RW (eds), Cerebral Vascular Disease, Eighth Princeton Conference on Cerebrovascular Diseases. New York, Grune & Stratton, 1973, pp 59-75
2. Walsh FB, Hoyt WF: Clinical Neuroophthalmology, 3rd ed. Baltimore, Williams & Wilkins, 1969, pp 2468-2480
3. Silver JR, Buxton PH: Spinal stroke. Brain 97: 539-550, 1974
4. Brierley JB, Adams JH, Graham DI, Simpson JA: Neocortical death after cardiac arrest: A clinical, neurophysiological and neuropathological report of two cases. Lancet 2: 560-565, 1971
5. Finklestein S, Caronna JJ: Outcome of coma following cardiac arrest (abstr). Neurology (Minneap) 27: 367-368, 1977
6. Bates D, et al: Prospective study of nontraumatic coma: Methods and results in 310 patients. Ann Neurol 2: 211-220, 1977