

# Electrocardiographic Changes and Myocardial Damage in Patients with Acute Cerebrovascular Accidents

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**SUMMARY** In 100 consecutive patients with acute cerebrovascular accident, due to cerebral thrombosis in 72, cerebral hemorrhage in 12, embolus in 6, and subarachnoid hemorrhage in 10, there were 90 who had electrocardiographic abnormalities during the first three days after admission, compared to 50% in a control group. The patients with cerebrovascular accident had a 7- to 10-fold higher incidence of ST segment depression, prolonged Q-T<sub>c</sub> interval and atrial fibrillation, and a 2- to 4-fold higher incidence of T wave inversion, conduction defects, premature ventricular beats and left ventricular hypertrophy. Patients who died had a 2-, 3- and 5-fold higher incidence of electrocardiographic evidence of recent myocardial infarction, atrial fibrillation and conduction defects than those who survived, but these changes occurred in only 5, 21 and 14% of all patients, and other electrocardiographic changes could not be correlated with mortality.

IT IS WELL KNOWN that patients who have cerebrovascular accidents have an increased incidence of electrocardiographic abnormalities.<sup>1</sup> This is due mainly to the association of arteriosclerotic cerebral and coronary artery disease, which have common risk factors. In addition, arrhythmias, myocardial infarction, and bacterial endocarditis may cause cerebrovascular accidents as a result of embolism or hypotension, and cerebrovascular accidents, particularly those due to cerebral or subarachnoid hemorrhage, may be followed by electrocardiographic changes, with<sup>2-6</sup> or without<sup>7-21</sup> post-mortem evidence of myocardial damage. In the present report, the incidence and significance of electrocardiographic changes in patients with cerebrovascular accident have been studied by recording the electrocardiogram and serum level of enzymes which may arise from cardiac muscle in 100 consecutive patients (48 males and 52 females) admitted for acute cerebrovascular accident and in a control group of 100 consecutive patients of similar age and sex admitted for carcinoma of the colon.

## Patients Studied

The diagnosis and etiology of cerebrovascular accident were determined by the history, physical examination, lumbar puncture, T<sub>c</sub><sup>99</sup> brain scan, electroencephalogram, and cerebral angiogram where indicated. Of the 100 patients with cerebrovascular accident, 12 had cerebral hemorrhage, 10 had subarachnoid hemorrhage, 6 had stroke attributed to cerebral embolus, and the remainder (72) had stroke attributed to cerebral thrombosis. Only patients with completed stroke, and none with transient ischemic symptoms, were included. Electrocardiogram and serum level of enzymes which may arise from cardiac muscle, including creatine phosphokinase (CPK), hydroxybutyrate dehydrogenase (HBDH), lactic dehydrogenase (LDH), and glutamic-oxaloacetic transaminase (GOT) were obtained during the first 3

During the first three days after admission 29 patients had elevation of serum enzymes which may be derived from cardiac muscle, particularly CPK, which was increased 6-fold, compared to 2-fold increases in HBDH, GOT, and LDH. Only 5 of these patients had electrocardiographic evidence of recent myocardial infarction. Patients with elevated serum CPK had a 2-fold higher incidence of ST segment depression, T wave inversion, conduction defects and atrial fibrillation than those with normal CPK, and a mortality of 66%, compared to 30%. Of 41 patients who died, 49% had elevated serum CPK, compared to 15% of 59 patients who survived. These differences were significant ( $P < 0.01$ ). Serum CPK was more frequently helpful than the electrocardiogram in evaluating the extent of cardiac damage and in predicting mortality. Patients with acute cerebrovascular accident should have repeated evaluation of serum CPK and the ECG, and be monitored for arrhythmias.

days after admission. Patients who had hypotension or anoxemia, or who required administration of vasopressor drug, during the first three days after admission were not included.

## Results

### Historical Factors

The patients with cerebrovascular accident had a higher incidence of history of cerebrovascular disease (29-fold), diabetes and ischemic heart disease (2- and 3-fold), and of hypertension and hypercholesterolemia (4- and 5-fold) than the control group (table 1).

### Electrocardiographic Changes

Ninety of 100 patients with cerebrovascular accident had an abnormal electrocardiogram at the time of admission, compared to 50 patients in the control group. The patients with cerebrovascular accident had a 7- to 10-fold higher incidence of ST segment depression, prolonged Q-T<sub>c</sub> interval and atrial fibrillation, and a 2- to 4-fold higher incidence of T wave inversion, conduction defects, premature ventricular beats and left ventricular hypertrophy (by voltage criteria) (table 2). Five of the patients with cerebrovascular accident had electrocardiographic evidence of a recent myocardial infarction, including the appearance of Q waves and elevation of ST segments. Five patients had tall T waves and 4 had U waves, despite normal serum levels of potassium, compared to none in the control group. The incidence of non-specific ST-T wave changes and of evidence of old myocardial infarction was the same in the two groups. There were no striking differences between the electrocardiogram of patients with cerebral thrombosis, cerebral or subarachnoid hemorrhage, and cerebral embolus, except that the latter had a higher incidence of atrial fibrillation (100%).

### Serum Enzymes

Twenty-nine of 100 patients with cerebrovascular accident had serum levels of CPK above the upper limit of normal of

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**TABLE 1** *Incidence of Certain Historical Features, Hypertension and Hypercholesterolemia in 100 Patients with Acute Cerebrovascular Accident and 100 Patients with Carcinoma of the Colon of Similar Age and Sex*

	Carcinoma of Colon	Cerebrovascular Accidents				
		Total	Cerebral Thrombosis	Cerebral Hemorrhage	Subarachnoid Hemorrhage	Cerebral Embolus
Number of Patients	100	100	72	12	10	6
Ischemic Heart Disease	15	39	32	6	1	0
Cerebrovascular Disease	1	29	28	0	1	0
Diabetes	7	16	16	0	0	0
Rheumatic Heart Disease	1	5	1	0	0	4
Cardiomyopathy	0	1	0	0	0	1
Cerebral Arteriovenous Malformation	0	1	0	0	1	0
Hypertension	12	48	36	5	5	2
Systolic Hypertension on Admission (>140 mm Hg)	18	65	48	9	5	3
Diastolic Hypertension on Admission (>90 mm Hg)	6	43	28	8	5	2
Hypercholesterolemia (>250 mg%)	6	30	23	2	4	1
Age (Years): Range	40-94	25-91	45-81	55-85	25-76	44-80
Mean	68	68	71	73	48	63

130 units, ranging from 145 to 2373 (median 306) units. (table 3). These included 20 of 72 patients with cerebral thrombosis, 2 of 10 with subarachnoid hemorrhage, 6 of 12 with cerebral hemorrhage, and 1 of 6 with cerebral embolus. The remaining 71 patients had serum levels of CPK between 2 and 130 (median 48) units. Other enzymes which may arise from cardiac muscle (HBDH, GOT and LDH) were also elevated in the group of patients with elevated serum CPK, though to a lesser degree (2 times the upper limit of normal or the level in patients with normal CPK). Elevated serum levels of CPK were not encountered in the control group.

#### Relation of Serum CPK to Electrocardiographic Changes

The 29 patients with elevated serum CPK had the same incidence of abnormal electrocardiogram (93%) as the 71 patients with normal levels (89%) (table 4). However, the incidence of ST segment depression, T wave inversion, conduction defects and atrial fibrillation in patients with elevated serum CPK was twice that in patients with normal levels. The five patients with electrocardiographic evidence of recent myocardial infarction all had elevated serum levels of CPK, but these were no higher than in other patients with elevated levels.

#### Mortality

Forty-one of 100 patients with cerebrovascular accident died during the period of hospitalization, 4 to 68 (mean 12) days after admission. These included 20 of 72 patients with cerebral thrombosis, all of 12 with cerebral hemorrhage, 6 of 12 with subarachnoid hemorrhage, and 3 of 6 with cerebral embolus. In 13 patients the cause of death appeared to be cerebral, in 11 cardiac, in 6 respiratory infection, and in 3 pulmonary embolus, while in 8 patients the final event was not clear. Mortality from cerebral causes usually occurred during the first week of hospital stay, whereas mortality due to infection or pulmonary embolus usually occurred later. Mortality from cardiac causes occurred with the same incidence during the first week or later.

#### Relation of Electrocardiographic Changes to Mortality

Of the 41 patients with cerebrovascular accident who died, 39 (95%) had an abnormal electrocardiogram on admission, compared to 86% of the patients who survived, a difference that was not significant (table 5). Those who died had a 2-, 3- and 5-fold higher incidence of electrocardiographic evidence of recent myocardial infarction, atrial fibrillation and

**TABLE 2** *Incidence of Electrocardiographic Changes in 100 Patients with Cerebrovascular Accident and 100 Patients with Carcinoma of the Colon of a Similar age And Size.*

	Carcinoma of Colon	Cerebrovascular Accidents				
		Total	Cerebral Thrombosis	Cerebral Hemorrhage	Subarachnoid Hemorrhage	Cerebral Embolus
Number of Patients	100	100	72	12	10	6
Abnormal Electrocardiogram	50	90	64 (89%)	12 (100%)	8 (80%)	6 (100%)
Left Ventricular Hypertrophy	8	23	17 (24%)	3 (25%)	3 (30%)	0 (0%)
Prolonged Q-Tc Interval	2	14	9 (12.5%)	3 (25%)	2 (20%)	0 (0%)
ST Segment Depression	3	22	14 (19%)	3 (25%)	4 (40%)	1 (16%)
T Wave Inversion	9	31	22 (30%)	4 (35%)	2 (20%)	3 (50%)
Non Specific ST-T Changes	24	22	18 (25%)	2 (16%)	1 (10%)	1 (16%)
Tall T Waves	0	5	2 (3%)	0 (0%)	3 (30%)	0 (0%)
U Waves	0	4	1 (1%)	2 (16%)	1 (10%)	0 (0%)
Old Myocardial Infarction	14	14	10 (14%)	2 (16%)	1 (10%)	0 (0%)
Recent Myocardial Infarction (Appearance of Q Waves etc.)	0	5	4 (6%)	1 (8%)	0 (0%)	0 (0%)
Conduction Defects	7	14	9 (12.5%)	3 (25%)	1 (10%)	1 (16%)
Atrial Fibrillation	2	21	10 (14%)	5 (41%)	0 (0%)	6 (100%)
Premature Ventricular Beats	3	13	10 (14%)	1 (8%)	0 (0%)	2 (33%)

TABLE 3 *Range and Median Values of Serum Enzymes (units per ml) in 100 Patients with Cerebrovascular Accident*

	Range of Normal Values	71 Patients with Normal Serum CPK		29 Patients with Elevated Serum CPK	
		Range	Median	Range	Median
CPK	0-130	3-130	48	145-2373	306
HBDH	180-330	180-849	297	220-3640	443
GOT	8-40	13-207	38	22-1500	62
LDH	100-200	130-352	227	147-1150	329

conduction defects than those who survived, but these changes occurred in only 5, 21 and 14% of all patients, and other electrocardiographic abnormalities could not be correlated with mortality. Two of 10 patients with normal electrocardiograms on admission died.

#### Relation of Serum CPK to Mortality

Of the 29 patients with cerebrovascular accident who had elevated serum CPK on admission, 66% died, compared to 30% of the 71 patients with normal serum levels (tables 4 and 5). Of the 41 patients with cerebrovascular accident who died, 49% had elevated serum CPK, compared to 15% of the 59 patients who survived. Of the 20 patients with cerebral thrombosis who died, 55% had elevated serum CPK, compared to 17% of the 52 patients who survived. These differences were all significant ( $p < 0.01$ ). Of the 12 patients with cerebral hemorrhage, all of whom died, 6 (50%) had elevated serum CPK. Of the 6 patients with subarachnoid hemorrhage who died, 2 (33%) had elevated serum CPK, compared to none of the 4 patients who survived. Of the 3 patients with cerebral embolus who died, one (33%) had elevated serum CPK, compared to none of the 3 patients who survived.

#### Illustrative Patient J.B.

A 26 year old white female, who had previously been in good health, was brought to the emergency room in coma. Three hours previously she had complained of pain and stiffness of the neck, and soon afterward vomited and then

became comatose. Physical examination showed an unconscious female with decerebrate rigidity and posture who did not respond to painful stimuli. Blood pressure was 200/100. Respiration was shallow and slow. Pupils were fixed and dilated. The Babinski reflex was positive bilaterally. Spinal tap revealed grossly bloody fluid which did not clear in successive tubes and which had a xanthochromic supernatant. The electrocardiogram on admission (fig. 1) showed sinus tachycardia, with a rate of 130/min., normal axis, prolonged QT<sub>c</sub> interval, tall peaked T waves, slight ST segment depression in leads 2, 3, and aVF and small, 3 mm Q waves in these leads, which may be normal for this age. On the second and third day of hospitalization, the electrocardiogram did not change except for inversion of the T wave in lead V<sub>2</sub>. On the first day of illness, the serum CPK was 408 units (upper limit of normal 130) and HBDH 3640 (upper limit of normal 330). The serum GOT and LDH were 30 and 180 on the first day, and rose to 45 and 250 units on the second day. The patient remained comatose. Endotracheal intubation was performed and respiration had to be supported mechanically after the first hospital day. The patient was not hypotensive or anoxicemic at any time, and required no vasopressor drug. On the third hospital day, after brain death was confirmed by flat electroencephalograms, the kidneys were removed for transplantation. Postmortem examination showed a ruptured intracranial aneurysm and subendocardial hemorrhages in the myocardium.

#### Illustrative Patient M.T.

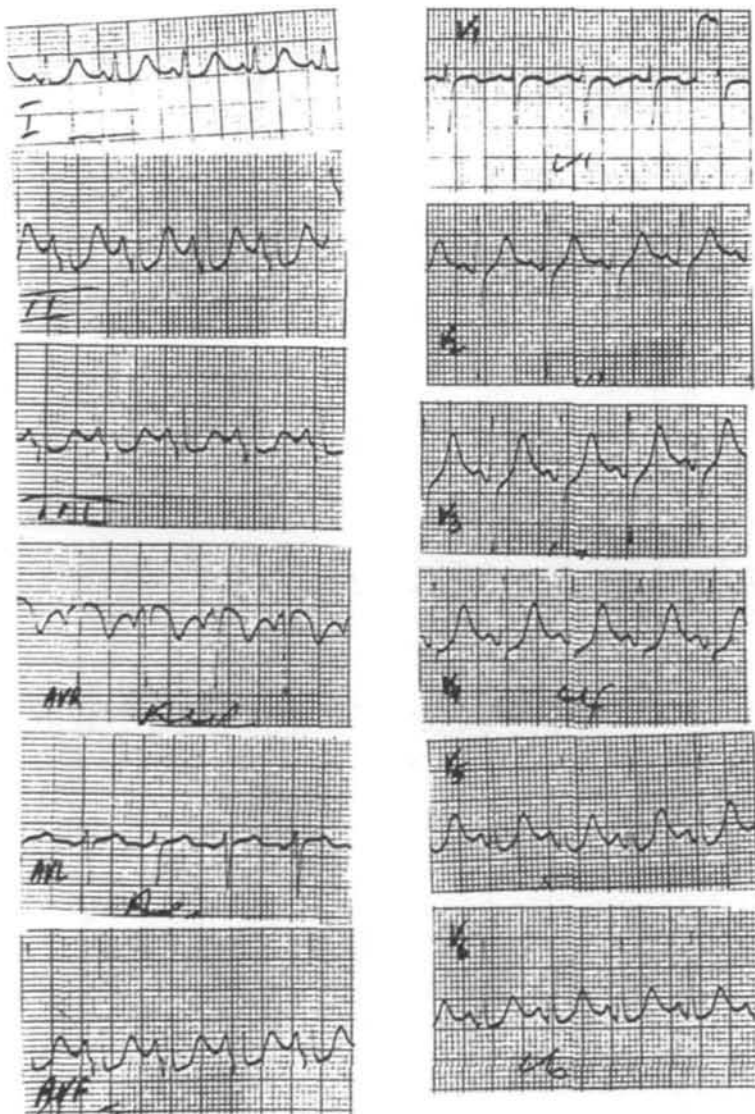
A 75-year-old white woman was admitted in coma. She had struck her head one day before and had progressively increasing headache during the day. Over a period of several hours she gradually lapsed into coma. There was a history of hypertension for 5 years. For several years she had experienced occasional syncopal episodes and drop attacks. Physical examination on admission showed the patient to be completely comatose, unresponsive, flaccid and areflexic. Pupils were fixed and widely dilated. The Babinski reflexes were negative. The patient became apneic and was promptly intubated and mechanically ventilated. Spinal tap showed an opening pressure of 150 mm H<sub>2</sub>O and grossly bloody fluid which did not clear. Blood pressure was 140/90 on admission and was within normal limits until shortly before death. The heart was enlarged on physical examination and on chest X-ray, and there was a small infiltrate at both lung bases. Electrocardiogram on admission (fig. 2) revealed normal sinus rhythm, non-specific ST segment depression in leads II, aVF, V<sub>4</sub> and V<sub>5</sub>, and the presence of U waves. On the next day, there was slight ST segment elevation in leads I and aVL with slight ST segment depression in leads II, aVF, V<sub>4</sub>, V<sub>5</sub> and V<sub>6</sub>, slight widening of QRS, and premature atrial

TABLE 4 *Relation of Electrocardiographic Changes to Serum Levels of Creatine Phosphokinase (CPK) in 100 Patients with Cerebrovascular Accident*

	Normal CPK	Elevated CPK
Number of patients	71	29
Abnormal electrocardiogram	63 (89%)	27 (93%)
Left ventricular hypertrophy	17 (24%)	6 (21%)
Prolonged Q-T <sub>c</sub> interval	11 (15%)	3 (10%)
Significant ST segment depression	13 (18%)	9 (31%)
T Wave inversion (more than one lead)	18 (25%)	13 (45%)
Non-specific ST-T changes	19 (27%)	3 (10%)
Tall T waves	2 (3%)	3 (10%)
U waves	2 (3%)	2 (7%)
Evidence of old myocardial infarction	10 (14%)	4 (13%)
Conduction defects	8 (11%)	6 (20%)
Atrial fibrillation	11 (15%)	10 (34%)
Premature ventricular beats	9 (13%)	4 (13%)
Evidence of recent myocardial infarction, including appearance of Q waves	0 (0%)	5 (13%)
Died in hospital	22 (30%)	19 (66%)

**TABLE 5** Incidence of Electrocardiographic Changes and Elevated Serum Levels of Creatine Phosphokinase (CPK) in 100 Patients with Cerebrovascular Accident, and Relation to Mortality

	Number of Patients												
	Cerebrovascular Accident			Cerebral Thrombosis			Cerebral Hemorrhage	Subarachnoid Hemorrhage			Cerebral Embolus		
	All	Surv.	Died	All	Surv.	Died	All Died	All	Surv.	Died	All	Surv.	Died
Total Number of Patients	100	59	41	72	52	20	12	10	4	6	6	3	3
Elevated serum CPK	29	9	20	20	9	11	6	2	0	2	1	0	1
Normal Electrocardiogram	10	8	2	8	6	2	0	2	2	0	0	0	0
Abnormal Electrocardiogram	90	51	39	64	46	18	12	8	2	6	6	3	3
Left Ventricular Hypertrophy	23	13	10	17	13	4	3	3	0	3	0	0	0
Prolonged Q-T <sub>c</sub> Interval	14	7	7	9	7	2	3	2	0	2	0	0	0
Significant ST Segment Depression	22	10	12	14	9	2	3	4	1	3	1	0	1
T Wave Inversion (more than one lead)	31	18	13	22	16	6	4	2	0	2	3	2	1
Non-Specific ST-T Changes	22	11	9	18	13	5	2	1	0	1	1	0	1
Tall T Waves	5	2	3	2	1	1	0	3	1	2	0	0	0
U Waves	4	0	4	1	0	1	2	1	0	1	0	0	0
Evidence of Old Myocardial Infarction	14	10	4	10	9	1	2	1	1	0	1	0	1
Evidence of Recent Myocardial Infarction	5	2	3	4	2	2	1	0	0	0	0	0	0
Conduction Defects	14	3	11	9	3	6	3	1	0	1	1	0	1
Atrial Fibrillation	21	7	14	10	4	6	6	0	0	0	6	3	3
Premature Ventricular Beats	13	10	3	10	9	1	1	0	0	0	2	1	1

**FIGURE 1.** Electrocardiogram of patient J.B. on admission.

beats (fig. 3). The patient developed paroxysmal supra-ventricular tachycardia. The serum enzyme levels determined on the first and second hospital days were CPK 115 and 528 units, HBDH 1,086 and 1,130 units, LDH 250 and 750 units, and SGOT 50 and 135 units. The blood pressure fell at the end of the third hospital day, responding only transiently to vasopressor drugs, and the patient died shortly thereafter. Postmortem examination showed the heart to be enlarged, weighing 420 grams, with left ventricular enlargement. There was scattered fibrosis, and areas of myocytolysis (fig. 4). The lungs showed atelectasis at both bases. The brain showed an extensive hemorrhage which had arisen in the cerebellum from rupture of an arteriosclerotic artery.

### Discussion

The interrelationship of cerebrovascular disease and cardiovascular disease has been repeatedly emphasized.<sup>22, 23</sup> They have common risk factors, such as hypertension, diabetes, hyperlipidemia, and cigarette smoking,<sup>24, 25</sup> and frequently coexist. Decompensation in one system may adversely affect the other, whether or not the patient has recognized disease of both systems. Cardiac disease may cause acute cerebral manifestations in several ways. Three to 8% (in the current study 6%) of acute cerebrovascular accidents are due to cerebral emboli, usually arising from a fibrillating auricle, or less often from a mural thrombus on a myocardial infarct or from endocarditis. Acute myocardial

infarction may be followed by transient or permanent neurologic damage as a result of acute reduction of cerebral blood flow due to hypotension or arrhythmia.<sup>26</sup> Heart block, bradyarrhythmias or tachyarrhythmias may cause transient cerebral symptoms or the Adams-Stokes syndrome.<sup>27-29</sup>

On the other hand, it is well known that patients with acute cerebrovascular accidents have a high incidence of electrocardiographic changes and of arrhythmias.<sup>30</sup> In the current study 90% of such patients had an abnormal electrocardiogram, compared to 50% of a control group. The incidence of ST segment depression, prolonged Q-T<sub>c</sub> interval and atrial fibrillation was 7- to 10-fold higher, and of T wave inversion, conduction defects, premature ventricular beats and left ventricular hypertrophy 2- to 4-fold higher. The association of cerebrovascular accident with myocardial infarction has been repeatedly described,<sup>31-34</sup> though only 5% of the patients with cerebrovascular accident in this study had electrocardiographic changes compatible with recent myocardial infarction. In the other patients with cerebrovascular accident who had an abnormal electrocardiogram, there was no electrocardiographic change that was not present in a smaller proportion of patients in the control group, with the exception of tall peaked T waves in 5 patients and U waves in 4, which were not present in the control group. However, these changes were not sufficiently frequent or distinctive to be of diagnostic help. Patients who died had a 2-, 3- and 5-fold higher incidence of electrocardiographic evidence of recent myocardial infarction, atrial fibrillation and

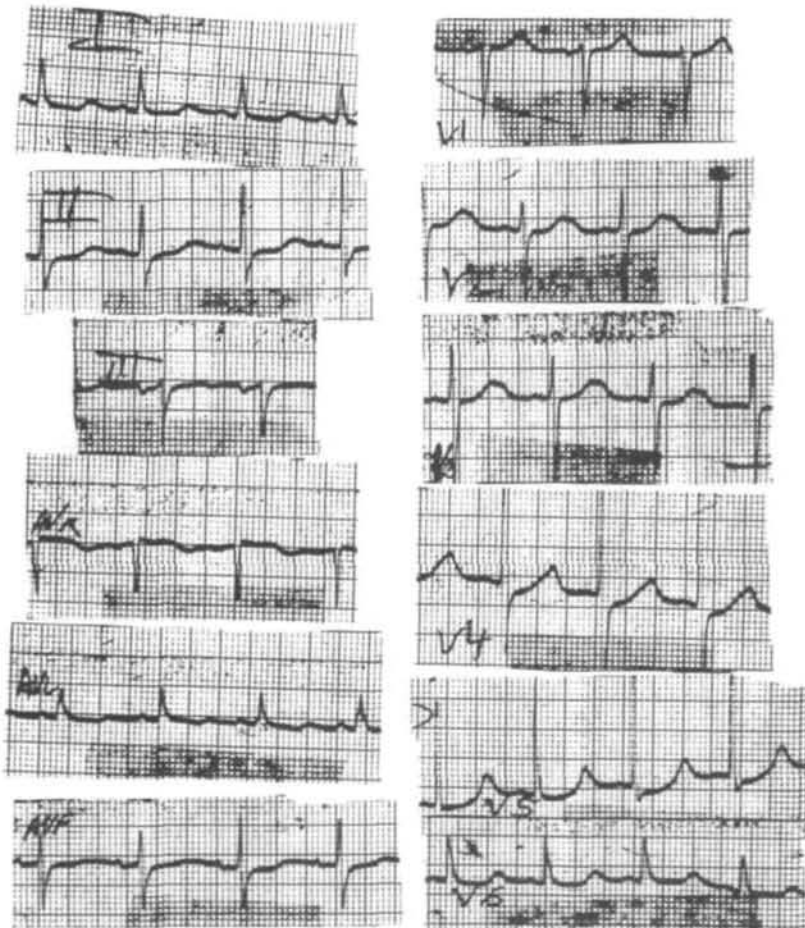


FIGURE 2. Electrocardiogram of patient M.T. on admission.



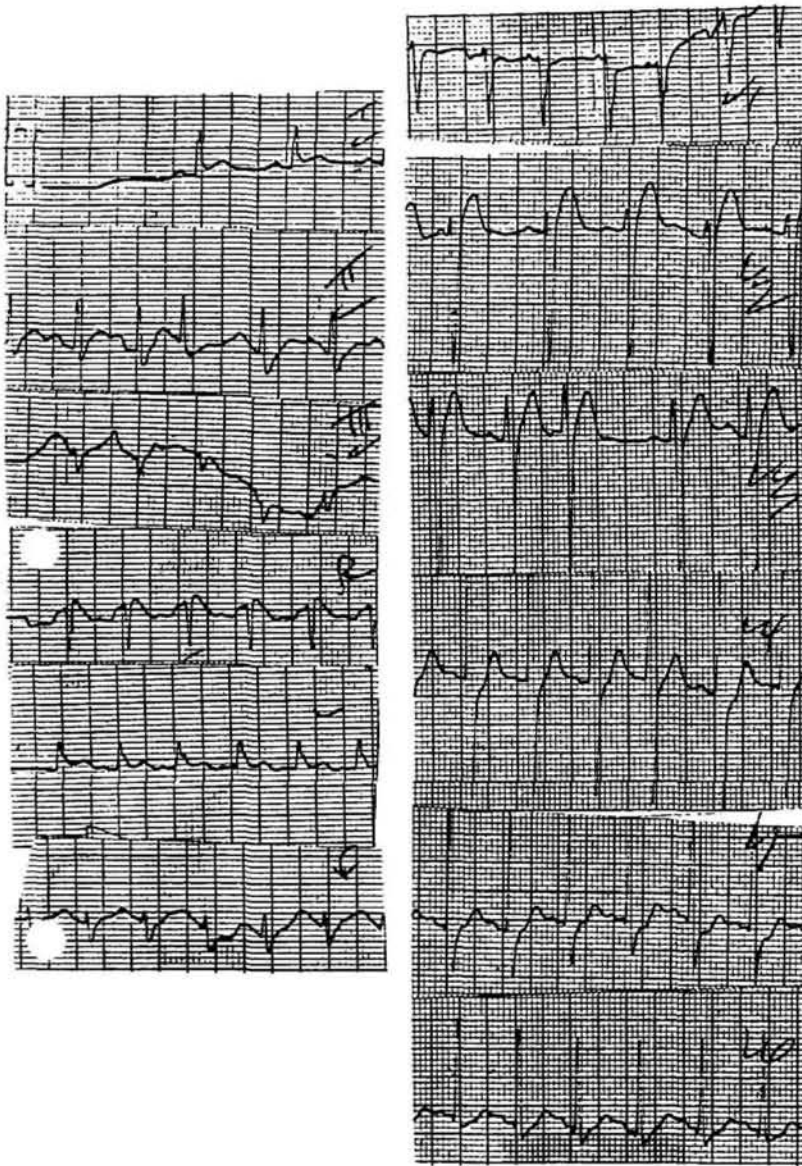


FIGURE 3. *Electrocardiogram of patient M.T. on second hospital day.*

conduction defects than those who survived, but these changes occurred in only 5, 21 and 14% of all patients, and other electrocardiographic changes could not be correlated with mortality. Therefore, the electrocardiogram of patients with cerebrovascular accident obtained on admission was usually of limited value in predicting mortality.

In view of the advanced age of the patients and common risk factors for cerebrovascular and cardiovascular disease, it is difficult in patients with cerebral thrombosis, hemorrhage or embolus to distinguish between pre-existing electrocardiographic changes and changes which might indicate cardiac damage resulting from the cerebrovascular accident. In the younger patients with subarachnoid hemorrhage due to berry aneurysm or arteriovenous malformation, the electrocardiographic changes that were observed can be more readily related to cerebral damage. These included ST segment depression in four patients, T wave in-

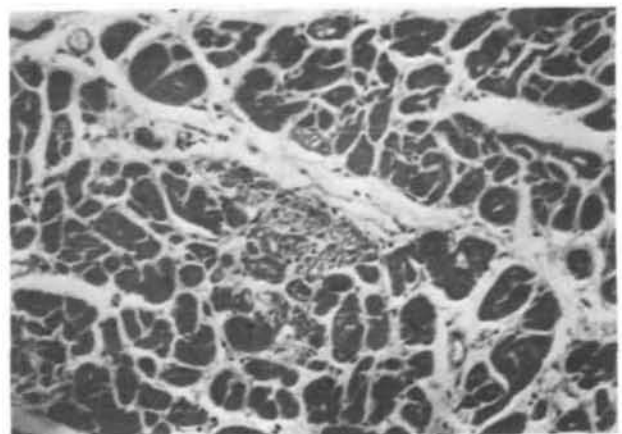


FIGURE 4. *Photomicrograph of section of heart, patient M.T., showing focal myocytolysis in the myocardium (H and E,  $\times 420$ ).*

version in two, prolonged Q-T<sub>c</sub> interval in two, tall T waves in three and U waves in one. These changes, and, rarely, ST segment elevation, have been previously described.<sup>7-21, 31</sup> In most patients who die of subarachnoid hemorrhage, including those with severe electrocardiographic changes detected prior to the occurrence of hypotension or anoxemia, the heart has been normal at post-mortem examination. This had led to the suggestion that the electrocardiographic changes may be neurogenic in origin. Electrocardiographic changes and arrhythmias have been observed following manipulation of the circle of Willis during surgical procedures,<sup>35</sup> and, in experimental animals following stimulation of certain areas of the central nervous system,<sup>36-39</sup> the vagus nerve,<sup>40</sup> or the stellate ganglion,<sup>41</sup> or following catecholamine infusion.<sup>42-44</sup> In some experiments the changes could be prevented by cervical cord transection,<sup>45, 46</sup> vagal block,<sup>47</sup> or propranolol administration,<sup>48</sup> and were attributed to interplay between sympathetic and vagal stimulation of the heart. On the other hand, some patients who died of subarachnoid hemorrhage were found to have subendocardial hemorrhages and focal areas of myocardial cell injury and myocytolysis.<sup>3-5</sup> The pathologic findings could not be correlated with the presence of electrocardiographic changes.<sup>5</sup> One patient had Q waves in the electrocardiogram, but autopsy revealed diffuse myocardial damage rather than myocardial infarction. Subendocardial hemorrhages have been reported in 40%,<sup>40</sup> and epicardial hemorrhages or myocytolysis in 8%<sup>6</sup> of patients who died from a variety of intracranial lesions. Similar histologic findings have also been reported following intracranial hemorrhage,<sup>50</sup> stimulation of the brain,<sup>5</sup> vagus,<sup>51</sup> or stellate ganglion,<sup>52</sup> or catecholamine infusion,<sup>53, 54</sup> in experimental animals. Acute myocardial infarction has been reported to occur following prolonged bilateral stimulation of the hypothalamus in cats.<sup>55</sup> These observations provide evidence that pathologic changes in the myocardium, as well as electrocardiographic changes, may result from cerebral injury and may be mediated by the autonomic nervous system. That the electrocardiographic changes observed in 8 of the 10 patients with subarachnoid hemorrhage might reflect myocardial damage was suggested by elevation of serum CPK and subendocardial hemorrhages or myocytolysis in 2 of these patients. A previous study reported elevation of serum CPK and SGOT in 8 of 20 patients with subarachnoid hemorrhage, and electrocardiographic changes in 6 of the 8.<sup>56</sup>

The level of serum enzymes that may arise from the heart was more frequently helpful than the electrocardiogram in evaluating the extent of cardiac damage and in predicting mortality in patients with cerebrovascular accident, regardless of cause. Of these enzymes, the serum level of CPK has proved to be the most useful indicator of myocardial damage.<sup>57</sup> Serum CPK arises almost entirely from cardiac or skeletal muscle, and minor elevation may follow intramuscular injections or other trauma to muscle. While smaller amounts of CPK are present in the brain,<sup>58</sup> the elevation of CPK in the serum that may occur following acute cerebral infarction<sup>59</sup> has been identified as muscle rather than brain isoenzyme,<sup>60</sup> is not accompanied by elevation of CPK in the spinal fluid,<sup>61</sup> and is not believed to arise from the brain.<sup>62</sup> Furthermore, intravenous administration to dogs of CPK isoenzyme which arises from the brain was followed by its

rapid disappearance from the blood.<sup>63</sup> Serum LDH and SGOT are derived not only from cardiac and skeletal muscle, but also from liver and other tissues, and are less helpful as indicators of myocardial damage. Elevation of  $\alpha$ -HBDH, which represents LDH isoenzymes LDH<sub>1</sub> and LDH<sub>2</sub>, may be helpful in the detection of myocardial injury, particularly when accompanied by an elevated ratio of HBDH to LDH. However, this may also occur in other diseases such as megaloblastic anemia, renal infarction, liver disease, and some myopathies and malignancies,<sup>60</sup> and is, therefore, less helpful as an indicator of myocardial damage than elevation of serum CPK.

Of 100 patients with acute cerebrovascular accident, 29% had serum levels of CPK that were above the upper limit of normal, with a median level 2½ times the upper limit of normal and 6 times the level in patients with normal CPK. Serum HBDH, GOT and LDH were increased in these patients to a median level 2 times the upper limit of normal or the level in patients with normal CPK. Only 5 of the 29 patients had electrocardiographic evidence of recent myocardial infarction. In the remainder, the electrocardiographic changes were qualitatively similar to those in patients with normal CPK, but there was a two-fold higher incidence of ST segment depression, T wave inversion, conduction defects and atrial fibrillation. The mortality of the 29 patients with elevated serum CPK (66%) was over twice that of patients with normal CPK (30%), and in the 41 patients who died, the incidence of elevated serum CPK (49%) was three times that in patients who survived (15%), regardless of whether the cerebrovascular accident was due to cerebral thrombosis or embolus or to subarachnoid hemorrhage. While the terminal event appeared to be cardiac in only one-fourth of the patients, the precise cause of death was not always clear, and the occurrence of elevated serum CPK in half the patients who died suggests that myocardial damage may have been a contributory factor in many of these patients. Electrocardiographic evidence of recent myocardial infarction, conduction defects, or atrial fibrillation indicated a poorer prognosis,<sup>31</sup> but the serum level of CPK was more frequently helpful than the electrocardiogram in predicting mortality. It is evident that every patient with cerebrovascular accident, whether due to thrombosis, hemorrhage or embolus, should have repeated evaluation of serum CPK and of the electrocardiogram, as a guide to prognosis and management, and should be monitored for arrhythmias, preferably in an acute care unit.

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