Acute Coronary Insufficiency Due to Acute Hemorrhage: An Analysis of One Hundred and Three Cases

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The occurrence of 59 cases of acute coronary insufficiency among 103 patients with acute hemorrhage, chiefly from the gastrointestinal tract, emphasizes the frequency and gravity of this generally unrecognized complication of bleeding. Clinical, electrocardiographic and anatomic manifestations of myocardial ischemia and subendocardial necrosis are prone to appear in previously diseased hearts, although they may develop in otherwise normal hearts. Consequently, prompt and adequate blood replacement is required in patients with coronary arteriosclerosis, enlarged hearts, valvular heart disease, etc. to prevent as well as to treat coronary insufficiency secondary to hemorrhage.

The concept of acute coronary insufficiency has become well established on the basis of clinical and pathologic observations. It has been shown that myocardial ischemia results from a disproportion between the oxygen requirements of the myocardium and the coronary blood flow, and is provoked by factors which either increase the work of the heart, decrease coronary blood flow or decrease the quantity of oxygen carried by the blood. When cardiac ischemia is severe or prolonged, myocardial necrosis may develop in the absence of acute coronary occlusion. The necrosis following acute coronary insufficiency is focal, disseminated and usually localized to the subendocardial region of the left ventricle, especially within the papillary muscle. The electrocardiogram is characterized by the presence of RS-T segment depression and T-wave inversion in one or more leads and often in all leads. These changes are usually transient and disappear rapidly following subsidence of the ischemia. Deep Q waves and elevations of the RS-T segment almost never occur, thus differentiating this condition from massive infarction due to acute coronary artery occlusion.

The clinical factors which may lead to acute coronary insufficiency have been enumerated previously. We have found hemorrhage to be one of the most frequent and important precipitating causes of acute coronary insufficiency. In a patient whose coronary circulation is already impaired by arteriosclerosis or by cardiac hypertrophy, hemorrhage from any source offers dangerous potentialities. It is not sufficiently appreciated that bleeding is important not only because of loss of an essential transport agent for oxygen and food but also because of the cardiac damage which may ensue.

Material and Results

This report is based on a clinical analysis of 103 consecutive cases of moderate or severe hemorrhage admitted to the Mount Sinai Hospital. Included in the series were those patients in whom evidences of hemorrhage were considered to be of sufficient degree to require treatment and from whom one or more electrocardiograms were made during the course of hemorrhage.

The gastrointestinal tract was the source of bleeding in 85 patients, the uterus in 4, the prostate gland in 2, and a ruptured aorta in 2. The most common etiologic factor for massive gastrointestinal hemorrhage was peptic ulcer (64 cases). Less common causes were esophageal varices (10 cases), ulcerative colitis (8 cases) and hemorrhoids (8 cases).

The clinical course of each patient was studied with particular regard to the amount and rapidity of hemorrhage, hemoglobin level, heart rate, blood pressure, presence of shock, and the electrocardiographic findings. The 103 cases were divided into two general groups. Group I consisted of 59 cases (57 per cent) with clinical or electrocardiographic signs of acute coronary insufficiency. Group II comprised 44 cases (43 per cent) with neither clinical nor electrocardiographic evidence of coronary insufficiency. Group I could be subdivided into 32 cases with an electrocardiographic pattern of acute coronary insufficiency but no clinical stigmata, 6 cases with clinical findings of coronary insufficiency but normal electrocardiograms and 21 instances...
with both clinical and electrocardiographic abnormalities.

Twenty-two patients died of the effects of the hemorrhage; of these, 18 presented clinical or electrocardiographic signs of acute coronary insufficiency. Four of the 13 autopsied cases presented cardiac alterations characteristic of acute coronary insufficiency; namely, myocardial necrosis in the absence of recent coronary artery occlusion.

**Discussion**

**Clinical, Electrocardiographic and Anatomic Features**

**Clinical Signs of Coronary Insufficiency.** Clinical signs of acute coronary insufficiency were noted in 27 patients, in 21 of whom acute electrocardiographic changes were observed. The electrocardiogram in the other 6 remained unaltered. Precordial or substernal pain occurred in 15 cases, congestive heart failure developed in 8, and both pain and cardiac failure together appeared in 3 instances.

The precordial pain often resembled that seen in coronary artery disease. In 6 patients, severe precordial pain in association with shock, tachycardia and drop in blood pressure which followed the hemorrhage closely simulated acute coronary artery occlusion. Indeed, this diagnosis was entertained not infrequently before it was recognized that precordial pain could be a manifestation of acute coronary insufficiency precipitated by hemorrhage.

Heart failure during or following hemorrhage was observed in 11 cases and was manifested by dyspnea, pulmonary congestion or edema, peripheral venous engorgement and gallop rhythm. Acute pulmonary edema of sudden onset was not uncommon and constituted still another feature which caused the clinical picture to resemble that of acute coronary artery occlusion.

Precordial pain and heart failure occurred, as a rule, in the patients with severe acute anemia or shock. The average hemoglobin level in these cases was 44 per cent (Sahli), while the actual drop in hemoglobin averaged 37 per cent from control levels. Similarly, shock, together with a marked fall in blood pressure and tachycardia, occurred in over two-thirds of the patients (60 per cent).

The precordial pain and the heart failure were generally transient, subsiding as the hemorrhage ceased or was actively treated and as the shock diminished and the blood hemoglobin rose toward normal levels, usually after one or more transfusions. The response to treatment was particularly striking in several cases of recurrent hemorrhage in which each bout of blood loss had precipitated an episode of severe angina pectoris. It was significant that angina pectoris was absent or mild in the periods between the occurrence of hemorrhage, and in each instance subsided rapidly following active treatment of the bleeding.

**Electrocardiographic Findings.** Significant acute changes in the electrocardiogram were present in 53 of the 103 patients. These consisted generally of flattening or inversion of the T wave, with or without depression of the RS-T segment. Abnormal T waves alone were observed in 24 cases, RS-T depression alone in 4 and combined RS-T and T changes in 25 cases. The mortality rate of the 24 cases showing T wave changes alone was only 17 per cent as compared with a rate of 40 per cent in the 25 patients who had presented RS-T depression in association with T-wave changes. It seems, therefore, that a combination of RS-T segment depression and T-wave inversion represents a more profound degree of coronary insufficiency than a change in the T wave alone. There were but 4 patients in whom changes were limited to the RS-T segment, and 3 of these patients died (fig. 1).

The most common lead combinations showing the RS-T and T wave changes were I, II and IV; I, II and III; and I, II, III, IV, respectively. Abnormalities were disclosed most frequently in Leads I and II.

The T-wave changes consisted of flattening and partial or complete inversion. The RS-T segment was depressed from 0.5 to 2.0 millimeters. RS-T elevation was observed infrequently in Lead III but never in any of the other leads. Deep Q waves were also extremely rare and developed in but 3 cases. Occasionally a deep Q wave was present prior to the episode of hemorrhage, and was the result of infarction due to a former coronary artery occlusion. The relative rarity of RS-T elevation and deep Q waves was of aid in differentiating the electro-
cardiogram of acute coronary insufficiency from that of myocardial infarction due to acute coronary artery occlusion.

Influence of Sex and Age. The series included 78 men and 25 women. Forty-one of the former (53 per cent) and 18 of the latter (72 per cent) developed evidence of acute coronary insufficiency. The mortality rate in each sex group was exactly the same.

The ages of the patients with hemorrhage who developed acute coronary insufficiency varied greatly (from 18 to 79 years). Similarly, the ages of those without coronary insufficiency ranged from 22 to 89 years. It appeared that age itself did not significantly influence the incidence of acute coronary insufficiency in this series. Acute coronary insufficiency developed, not infrequently, in the very young if the hemorrhage was sufficiently severe or protracted. Thus, one instance of myocardial necrosis was observed in a girl of 19 in whom the coronary arteries were perfectly normal. On the other hand, some of the elderly patients presented no significant signs of coronary insufficiency even after fairly severe hemorrhage. The average age of the men who developed coronary insufficiency was 52, and that of the women was 45 years.

Antecedent Cardiac Disease. Antecedent cardiovascular disease proved to be a more significant factor than age in the occurrence of coronary insufficiency following hemorrhage. Thirty-eight of the 103 patients presented clinical or electrocardiographic evidence of previous cardiovascular disease, generally of the hypertensive or arteriosclerotic variety. Seventy-one per cent of these 38 patients developed acute coronary insufficiency as compared with an incidence of 49 per cent in the group without preceding cardiovascular disease. Further analysis revealed that the association of antecedent cardiovascular disease was approximately twice as great in the coronary insufficiency group (47 and 25 per cent, respectively). These observations indicate that chronic coronary insufficiency incident to coronary arteriosclerosis or cardiac hypertrophy renders the heart more vulnerable to the hemodynamic effects of hemorrhage.

Blood Hemoglobin Level. The blood hemoglobin concentration at the time that the clinical or electrocardiographic signs of coronary insufficiency had developed were tabulated and the actual decrease in hemoglobin determined by comparison with the level prior to the hemorrhage or following recovery. The average hemoglobin concentration for the group with evidence of coronary insufficiency was 54 per cent of normal (Sahli). That of the noncoronary insufficiency group was 63 per cent. When only those cases were considered in which symptoms of coronary insufficiency had developed, the average hemoglobin level was found to have been 44 per cent of normal. The number of patients who had sustained a drop in hemoglobin level of 20 to 30 per cent or more was distinctly greater in the coronary insufficiency group. Conversely, it was found that when the hemoglobin level had decreased 30 per cent or more, acute coronary insufficiency appeared in four-fifths of the patients.

In general, therefore, acute coronary insufficiency occurred when the hemorrhage effected a significant drop in blood hemoglobin. Nevertheless, acute coronary insufficiency was noted, not infrequently, before any significant anemia.
had developed and, occasionally, even if such had never appeared. Thus, severe precordial pain associated with acute electrocardiographic changes occurred in 3 patients whose hemoglobin level dropped only 10 per cent or less. In these patients the hemoglobin level might not have been an accurate measure of the severity of hemorrhage because of hemoconcentration. It is evident, accordingly, that acute anemia is an important but not an essential force for the production of acute coronary insufficiency in hemorrhage. In the absence of anemia, the factors of shock, drop in blood pressure and tachycardia take on additional importance in precipitating coronary insufficiency.

The electrocardiogram seemed to be a sensitive indicator of the intensity of bleeding. Alterations in the electrocardiogram often were noted long before clinical manifestations of coronary insufficiency appeared and in some cases even when other clinical signs were wanting.

**Blood Pressure.** The average fall in blood pressure at the time the electrocardiogram was obtained was 27 mm. Hg in the coronary insufficiency group as contrasted with only 9 mm. in the group without signs of coronary insufficiency. Further, one-third of the former had shown a drop in blood pressure of 40 mm. or more as compared with only 5 per cent of the latter group. A significant drop in blood pressure following a bleeding episode proved to be an important precipitating factor of coronary insufficiency. This belief is supported by the observation that the incidence of coronary insufficiency was 84 per cent when the blood pressure fell 20 mm. or more and 90 per cent when the fall was 40 mm. or more. A drop in blood pressure was thus directly related to the presence of coronary insufficiency as indicated by electrocardiograms and by clinical signs.

**Tachycardia.** Tachycardia of 100 beats or more per minute was noted in 52 per cent of the patients with coronary insufficiency and in only 14 per cent of the other group. Conversely, 82 per cent of the patients with heart rates of 100 or more manifested stigmata of coronary insufficiency. Evidence of coronary insufficiency was noted in the 10 instances (17 per cent of the group) in which the heart rate rose to 125 or more. Such a rapid rate never occurred in those patients without signs of myocardial ischemia.

In the coronary insufficiency group, tachycardia generally accompanied a marked drop in blood pressure. Although tachycardia represents a compensatory mechanism for the maintenance of cardiac output following blood pressure fall, the combination of hypotension and tachycardia apparently led more readily to the development of coronary insufficiency.

**Shock.** Clinical manifestations of shock (syncope, prostration, feeble pulse, clammy skin, etc.) were observed in 38 per cent of the coronary insufficiency group but only in 20 per cent of Group II. The incidence of shock was found to be as high as 69 per cent in the 27 patients with signs of coronary insufficiency. Moreover, of the 43 patients who developed signs of shock, 79 per cent manifested myocardial ischemia. These figures emphasize the close relationship between shock and coronary insufficiency following hemorrhage. The coexistence of a fall in blood pressure and tachycardia was noted frequently in the majority of patients with shock. As one would expect, shock was more common in the patients with coronary insufficiency who succumbed (82 per cent) than in those who recovered (48 per cent).

In summary it can be said that a fall in blood hemoglobin and blood pressure, tachycardia and shock are all significant forces in precipitating coronary insufficiency following hemorrhage. When the bleeding episodes were accompanied by any one or more of these clinical findings, acute coronary insufficiency developed in at least four out of every five cases.

A typical example of coronary insufficiency is illustrated in the following case.

**Case 2.—**H. C., a 38 year old man with a duodenal ulcer, was hospitalized because of a moderate gastrointestinal hemorrhage of two weeks' duration. For one week prior to entry he had experienced dyspnea and squeezing precordial pain which had radiated to the left shoulder and arm following exertion. Hypertension had been present for eight years with no diminution of cardiac reserve; blood pressure varied between 150–170 mm. systolic and 100–110 mm. Hg diastolic.

Upon admission, July 19, 1941, there was no shock, tachycardia or fall in blood pressure. The hemoglobin level was 65 per cent. The electrocardio-
gram (fig. 2), July 21, showed inversion of the T wave in Leads I, II, and III. With cessation of the bleeding and as the hemoglobin level rose, angina pectoris disappeared and the electrocardiogram showed a gradual return to normal. On July 23 the hemoglobin was 74 per cent; the electrocardiogram disclosed the T wave to be low in Leads I and II and upright in Lead III. On July 28, the hemoglobin was 78 per cent while the electrocardiographic pattern was normal. Subsequent to discharge from the hospital, the 2-step test electrocardiogram was also normal.

Comment: A case of acute coronary insufficiency with clinical and electrocardiographic manifestations occurring in a hypertensive man during the course of a moderately severe and protracted gastrointestinal hemorrhage. Following treatment of the anemia, there was rapid disappearance of angina pectoris and restoration of the electrocardiogram to normal.

Anatomic Findings. The myocardium in patients with coronary insufficiency due to acute blood loss presents a pathologic picture similar to that seen in instances of acute coronary insufficiency due to other causes. The degree of morphologic changes depends upon the severity and rapidity of the hemorrhage and the nature of the underlying predisposing factors. Following acute severe hemorrhage, the myocardium of patients with coronary arteriosclerosis, cardiac hypertrophy or aortic valvular disease, for example, will be more seriously affected than that of a patient with no previous heart disease. The rate of blood loss, duration of the

Fig. 2.—H. C., a man of 38 years. Transient anginal syndrome and acute coronary insufficiency during gastro-intestinal hemorrhage. Hemoglobin fell only to 65 per cent. Upon admission to hospital, July 21, 1941, the T wave in Leads I, II, and III was inverted; normal within a week.
nuclear degeneration to actual necrosis with reactive cellular infiltration. Finally, in the most pronounced cases, confluent zones of sub-endocardial necrosis are grossly recognizable.

Thirteen cases came to autopsy, but only 7 hearts were available for re-examination by the writers. These included all 4 positive cases and 3 of the negative cases. All grossly visible coronary arteries were studied by transverse sections at intervals of 2 to 3 mm. In no instance was an acute coronary artery occlusion found. Microscopic studies were made routinely from all representative portions of heart wall; namely, anterior, posterior and lateral walls, septum, apex, anterior and posterior papillary muscles of the left ventricle, anterior and posterior walls of the right ventricle, and auricles when indicated. In addition, any area disclosing discoloration or mottling was examined historically.

The variety of cardiac lesions may be noted in the following illustrative cases.

Case 3.—H. S., a 67 year old woman with clinically recognized aortic stenosis presented the most extensive myocardial changes we have observed, in the absence of an acute coronary artery occlusion, following gastrointestinal hemorrhage. Since 1940 the patient had experienced angina pectoris precipitated by repeated bouts of gastrointestinal hemorrhage. During these periods the blood hemoglobin level dropped to 40–50 per cent, and the electrocardiogram would disclose pronounced RS-T segment depression and T-wave inversion (fig. 3, A). When the hemoglobin rose above 60 per cent following therapy, the angina pectoris subsided and the electrocardiogram would improve. The patient was again hospitalized on November 1, 1942, because of gastrointestinal bleeding for eight days and precordial pain for four days. Her blood pressure upon entry was 90/60, pulse rate 120 and hemoglobin 42 per cent. On the following day she suddenly developed the clinical picture of shock and pulmonary edema and died. The electrocardiogram disclosed a supraventricular tachycardia of 170; marked RS-T depression in Leads I, II and IV; and a deep Qr.

Cardiac Findings: The heart weighed 575 grams and was dilated. The left ventricle was moderately hypertrophied. Widespread necrosis was noted grossly in all portions of the left ventricle, including the papillary muscles. The zone of necrosis involved the inner third of the thickness of the ventricular wall, while the outer two-thirds of the wall, including the epicardium, were intact. The endocardium itself appeared normal, and no mural thrombi were observed. The affected areas disclosed yellowish mottling with scattered red foci, the latter especially noticeable within the septum and posterior wall. The right ventricle showed merely slight fatty infiltration.

The aortic valve was rigidly thickened, irregularly nodular and calcified; the aortic orifice severely stenotic. The mitral valve leaflets were moderately thickened; the mitral ring was markedly calcified. The coronary ostia were patent. The left circumflex coronary artery and its branches to the anterior left ventricle were moderately narrowed by arteriosclerotic plaques, while the remaining major branches of the coronary arteries disclosed only slight mural thickening. Detailed transverse sectioning of the entire coronary artery tree revealed no evidence of either a recent or old occlusion.

The microscopic picture was similar in all the involved regions (fig. 3, B). The endocardium was unaltered. Disseminated focal and often confluent areas of myonecrosis were present in the subendocardial layer, among which many islands of normal heart muscle remained. Frequently a very thin strip of uninvolved muscle was interposed between the endocardium and the zone of myonecrosis. The altered portions of myocardium disclosed homogenization, loss of striations, intiatorial changes, karyolysis, loss of nuclei, and conspicuous necrosis of muscle fibers. Interspersed were foci of hemorrhage and scattered cellular infiltrates consisting of polymorphonuclear leukocytes, lymphocytes and histiocytes.

The anatomic diagnoses were: acute, widespread, focal and confluent subendocardial necrosis of left ventricle; inactive rheumatic aortic and mitral valvulitis with severe aortic stenosis and moderate mitral stenosis and insufficiency; moderate coronary arteriosclerosis with narrowing of the lumen.

Comment: A patient in whom angina pectoris occurred during episodes of gastrointestinal bleeding developed extensive subendocardial necrosis of the myocardium. Rheumatic cardiovalvular disease, as well as coronary arteriosclerosis, acted as predisposing factors. Hemorrhage, with resulting hypotension, tachycardia and shock, occurred and precipitated acute coronary insufficiency.

Case 4.—S. S., a 60 year old man was observed in two bouts of severe hematemesis due to a chronic peptic ulcer. The first episode occurred on September 10, 1945, and was accompanied by shock, a blood pressure of 80/40, pulse rate of 120, poor heart sounds and hemoglobin of 30 per cent. The electrocardiogram on the day after admission showed semi-inversion of the T wave in Leads I and IV. On September 19, following several transfusions, the tracing was normal. In the second bout of hemorrage, which took place on January 17, 1946,
there was shock with a blood pressure of 90/50, tachycardia, poor heart sounds and a hemoglobin of 23 per cent. An electrocardiogram on January 21 revealed a low T wave in Lead I (fig. 4). On January

26 the patient developed agonizing substernal pain, dyspnea, cyanosis and severe shock and died within several hours. Electrocardiograms during this episode disclosed depression of the RS-T segment in Lead IV.

Cardiac Findings: The heart weighed 450 grams. Slight hypertrophy of the left and slight dilatation of both ventricles were noted but there were no gross myocardial changes. Moderate thickening of the mitral and tricuspid leaflets and slight thicken-

Fig. 4.—S. S., a man of 60 years with two bouts of hematemesis resulting from peptic ulcer. At autopsy, moderate coronary arteriosclerosis and acute, focal, subendocardial necrosis in both papillary muscles and posterior wall of left ventricle. On September 11, 1945, the hemoglobin was 30 per cent; the electrocardiogram disclosed inversion of the T wave in Leads I and IV. Following transfusions, clinical recovery and normal electrocardiogram resulted. On January 21, 1946, following hematemesis with shock and hemoglobin of 23 per cent, the electrocardiogram showed the T wave low in Leads I and IV. Five days later, the patient experienced agonizing substernal pain, and the RS-T segment was depressed in Lead IV; death followed.

Fig. 3.—H. S., a 67 year old woman with antecedent aortic and mitral valve disease, as well as coronary artery disease. Recurrent episodes of gastrointestinal bleeding precipitated seizures of angina pectoris. Extensive subendocardial myocardial necrosis of left ventricle at autopsy.

A. (Top) Electrocardiograms during the bouts of bleeding disclosed RS-T depressions and T-wave inversions in Leads I and II. During the second hemorrhage the T wave in Lead III and, during the third attack, in Lead IV, was, in addition, transiently inverted. The final episode of hemorrhage produced a supraventricular tachycardia, marked depressions of RS-T segment in Leads I, II, and IV and large Q wave in Lead III.

B. (Bottom) Photomicrograph of section from left ventricle. Subendocardial layer revealed disseminated focal and often confluent areas of acute myonecrosis. Occasionally a thin strip of uninvolved muscle was present immediately beneath the endocardium, interposed between the intact endocardium and the involved muscle. Homogenization, loss of striation, tinctorial changes, loss of nuclei, profound necrosis of muscle fibers, scattered hemorrhages and reactive cellular infiltration were observed.
dilated, as occasionally occurs despite the presence of arteriosclerotic plaques. Histologic changes were pronounced in scattered portions. The involved areas were focal and limited to the papillary muscles and subendocardial region of the posterior wall of the left ventricle. These consisted of tinctorial alterations, loss of striation, hemogenization and necrosis of myocardial fibers, together with a reactive infiltration composed principally of polymorphonuclear leukocytes.

The anatomic diagnoses were: acute, focal, subendocardial myonecrosis of posterior wall and papillary muscles of the left ventricle; focal myofibrosis; coronary arteriosclerosis without narrowing; inactive, moderate rheumatic valvulitis of the mitral, aortic and tricuspid valves.

Comment: Although the clinical picture during periods of severe gastrointestinal hemorrhage suggested acute coronary artery occlusion, the electrocardiograms were considered characteristic of acute coronary insufficiency. This impression was confirmed at autopsy by the presence of microscopic areas of focal, acute myonecrosis in the absence of acute coronary occlusion. Coronary arteriosclerosis and rheumatic valvular disease were predisposing factors to coronary insufficiency while severe bleeding, hypotension and shock constituted the precipitating mechanisms.

Case 5.—T. L., a 19 year old housewife with moderate rectal bleeding for two months due to ulcerative colitis, had had fever of 101 to 105° F. for three weeks, and a spontaneous miscarriage with moderate uterine hemorrhage one week prior to admission. She was disoriented, semistuporous and pale. The pulse rate was 128; respiratory rate varied from 30 to 40. The systolic blood pressure was 130; the diastolic could not be determined. The heart was not enlarged, the sounds were forceful, the rhythm regular; an apical presystolic gallop and a precordial systolic murmur were audible. Bilateral basal pulmonary rales were heard. The hemoglobin was 14 per cent, red blood cell count 885,000 per cu. mm., and leukocyte count 23,700 per cu. mm. of which 69 per cent were neutrophiles. The electrocardiogram (fig. 5) showed a depressed RS-T segment in Leads I, II, and III and flattened T waves in all leads. The patient improved slowly following transfusions; the hemoglobin rose to 32 per cent. However, one week after admission she suddenly passed numerous tarry stools and succumbed.
At autopsy, the heart weighed 225 grams. Beneath the endocardium of the trabeculae carneae and within the papillary muscles of the left ventricle were pale yellow streaks, while on section scattered areas of the musculature showed similar involvement. Microscopically, minute disseminated areas of ischemic change were noted within the subendocardial layers of the anterior and posterior walls of the left ventricle and within the papillary muscles. These were focal, pin-point areas of myocardial degeneration consisting of disappearance of nuclei, obscuration of myofibril outlines, foci of hemorrhage, necrosis and reactive acute and subacute inflammation.

Comment: Massive intestinal hemorrhage in a 19 year old girl suffering from anemia secondary to ulcerative colitis, resulted in focal myocardial necrosis in the wall of the left ventricle in the presence of normal coronary arteries and an otherwise normal heart.

Physiologic and Biochemical Considerations

It is pertinent to consider briefly the physiologic effects of hemorrhage upon the coronary circulation. Moderate blood loss causes a diminution in cardiac output, arterial blood pressure, circulating blood volume and venous return to the heart. These constitute the initiating factors in the vascular readjustments following acute hemorrhage. These alterations effect the vasopressor reflex, which in turn produces compensatory peripheral vasoconstriction, accelerates heart rate and tends to return blood pressure to normal. It is significant, however, that following the initial stage of reduced cardiac output and lowered blood pressure, a compensatory increase in cardiac output often occurs despite a decreased blood volume. This mechanism helps deliver a normal oxygen supply to the peripheral tissues by increasing circulation rate and oxygen utilization. It has been well established on clinical and experimental grounds that uncomplicated, severe hemorrhage may also produce a state of shock similar to that due to other causes.

Vasoconstriction generally is beneficial, helps maintain blood pressure and effect an adequate blood flow to vital organs. The question whether the coronary arteries participate in the generalized reflex vasoconstriction is of clinical importance. To such a possibility has been ascribed the development of acute coronary insufficiency as evidenced by electrocardiographic abnormalities, particularly following hemorrhage from the gastrointestinal tract. However, conclusive proof of such effect has not been adduced experimentally.

In continued bleeding all compensatory readjustments ultimately fail, the cardiac output is reduced strikingly with resultant irreparable damage to the cerebral vasomotor centers and cardiac muscle, and irreversible shock supervenes.

That the state of the myocardium contributes significantly to recovery from shock has been re-emphasized by Wiggers who has suggested that myocardial impairment rather than peripheral circulatory failure was responsible for the state of irreversible shock following hemorrhage. Lawson and Rehm have shown that when hemodilution has occurred in the terminal phases of post-hemorrhagic shock, the blood volume and venous pressure may be increased and the heart dilated, denoting myocardial damage and failure. Kohlstaedt and Page considered that cardiac dilatation is the critical point at which irreversible changes appear following hemorrhage, for up to this point infusion was therapeutically successful in their animals. In view of these observations, it would appear that the heart muscle is particularly susceptible to change in the presence of hemorrhagic shock and, in turn, exerts considerable influence in recovery.

An important consideration in a study of the effect of hemorrhage on the circulation is the quantity and rapidity of blood loss. It has been demonstrated that in the normal, average-sized man no serious effects appear if the hemorrhage is less than 30 per cent of the blood volume or less than 3 per cent of the body weight, i.e., less than 1,500 cc. of blood. On the other hand, in patients with organic heart disease, pulmonary disease, chronic anemia, etc., a loss of even 500 cc. of blood is tolerated poorly. The amount of blood loss, furthermore, has been related to electrocardiographic changes. Thus, Scherf and Klotz found no electrocardiographic abnormalities in two normal persons from whom 850 cc. and 400 cc. of blood, respectively, had been withdrawn. However, loss of even smaller quantities of blood proved to be
very significant in the presence of coronary artery disease or other factors predisposing to coronary insufficiency.

The rapidity of the fall may be of greater significance than the actual decrease in hemoglobin. In patients with chronic anemia who remain at rest, for example, the hemoglobin may fall to very low levels without producing evidences of coronary insufficiency. The compensatory mechanisms usually suffice to maintain normal coronary blood flow at rest. In active hemorrhage, on the other hand, if the hemoglobin concentration rapidly decreases 20 per cent or more, acute electrocardiographic changes frequently appear and occasionally anatomic myocardial alterations occur.

Biochemical studies following hemorrhage have yielded evidence of marked disturbances in tissue metabolism, involving electrolyte patterns and acid-base balance, with deleterious effects upon the coronary circulation and myocardium. In posthemorrhage shock there is also a striking reduction in tissue oxygen consumption, a mechanism which may be as important a cause of tissue anoxia as the reduced blood flow.

Clinical Observations of Coronary Insufficiency and Myocardial Involvement following Hemorrhage

As long ago as 1842, Hall wrote: “Hemorrhage not only induces syncope, but occasionally sudden death, due to interruption of the coronary blood supply. . . . Impaired coronary circulation may arise from impeded flow of blood through arteries contracted by ossification, or impeded by adipose substances. . . or from an insufficient condition of blood itself in cases of hemorrhage and anemia.”

The significance of the relationship between hemorrhage and cardiac sequelae, first suggested by Hall, was not generally recognized until the 1930’s, when Dietrich and Schwiegl, Bühner, and Goldenberg and Rothberger showed that anoxemia constituted an important precipitating cause of acute coronary insufficiency. Hicks later demonstrated that cardiac muscle, unlike skeletal muscle, is unable to go into temporary oxygen debt when the coronary circulation is impaired. Since that time the importance of cardiac muscle damage following blood loss has been emphasized repeatedly by investigators abroad and in this country. Friedberg and Horn found hemorrhage to be responsible for myocardial necrosis in 2 of their 34 cases of myocardial infarction without coronary artery occlusion and offered the opinion that the factor of shock was most important. Master, Jaffe and Dack described an instance of extensive myocardial infarction following severe gastrointestinal hemorrhage. Similar experiences were reported by Bean, Gross and Sternberg, McLaughlin, Baker and Sharpe, and Master, Gubner, Dack and Jaffe. On the basis of these and his own observations, Master emphasized the importance of hemorrhage as a cardiac emergency and urged early and repeated transfusions to forestall the development of coronary insufficiency. Additional clinical reports have appeared more recently.

The belief that hemorrhage exerts an important deleterious effect upon the myocardium is fortified by the clinical observations that heart failure either may be induced or worsened by hemorrhage. Heart failure was precipitated in 10 per cent of the cases included in this report. These observations emphasize the fact that hemorrhage is dangerous in patients with heart disease, and is of especially serious omen in those already in cardiac failure. Here both the cardiac failure and hemorrhage demand energetic treatment.

Electrocardiographic Considerations

The Electrocardiogram and Experimentally Induced Coronary Insufficiency. A number of observers have reported that, following severe or repeated bleeding of normal dogs and rabbits, flattening and inversion of the T waves and depression of the RS-T segments appeared. Tachycardia often developed. These changes were found similar to those observed in man during an attack of angina pectoris and in induced anoxemia. Presumably both diminished coronary flow and anoxemia might be responsible for the abnormal electrocardiogram following experimental bleeding in animals.

Electrocardiographic Changes due to Subendo-
cardial Involvement. In acute coronary insufficiency due to any cause, proof has been established of the relationship of the characteristic electrocardiographic changes, i.e., RS-T depressions and T-wave inversions, to localization of the myocardial necrosis within the subendocardium and papillary muscles.7, 3, 9, 31, 32, 63–72 Pruitt, Barnes and Essex,71 and Pruitt and Valencia72 described RS-T depression associated with experimentally produced lesions in the subendocardium of animals. Scherf and his colleagues51, 62 reported transient T-wave and RS-T changes in cases of profuse gastric hemorrhage, which they attributed to reflex coronary artery spasm. The occurrence of focal necrosis limited to the subendocardium and papillary muscle was postulated since the electrocardiographic patterns resembled those produced by experimental injury to the inner surface of the heart.64 These investigators observed that the more acute the loss of blood, the more marked were the electrocardiographic changes. It was their belief, moreover, that the electrocardiographic changes after acute hemorrhage were limited usually to the T wave and that only in severe cases did depression of the RS-T segment occur. They showed, further, that RS-T segment depression is regularly observed when anoxemia of the myocardium is widespread. Oerning, Sommerfelt and Fredriksen72 described T-wave changes and RS-T depressions in more than one-third of their 74 patients in whom hemorrhage had occurred and thought that the electrocardiographic alterations were due to vasomotor reflexes affecting the coronary circulation and the myocardial anoxemia which followed. Our studies confirm the belief that the abnormal electrocardiographic pattern is due, primarily, to the involvement of the subendocardial region of the left ventricle.

The electrocardiogram may afford sensitive and objective evidence of coronary insufficiency. Alterations in the T wave appear readily following blood loss in bed patients, and it appears that especially when RS-T depressions co-exist, the presence of acute coronary insufficiency is to be assumed whether or not clinical signs have been detected. We have observed patients showing RS-T segment depressions who gave no other indication of cardiac impair-ment and, yet, in whom an unusual physical effort induced myocardial collapse.

Additional details of our electrocardiographic findings will be reported subsequently. However, one observation seems worthy of comment here. Although T-wave inversion and depression of the RS-T segment are characteristic of the electrocardiogram following hemorrhage, as in other forms of acute coronary insufficiency, in 3 instances a deep Q wave ultimately appeared. These patients died. Permission for an autopsy examination was obtained in one case only (Case 3); widespread subendocardial necrosis was found in the absence of a recent artery occlusion. On the basis of this and other experiences, it is reasonable to assume that the coronary circulation had been reduced to such a degree previously that widespread myocardial necrosis followed the massive hemorrhage, and was responsible for the appearance of large Q waves in the electrocardiogram. In bleeding patients, the development of large Q waves in a tracing hitherto distinguished only by the presence of RS-T depression and T-wave inversions may signify extensive myocardial necrosis and antecedent heart disease.

Active therapeutic measures are indicated as soon as T-wave or RS-T segment alterations appear in the electrocardiogram. In our opinion a progressive decrease in amplitude of the T wave is sufficient proof that the loss of blood has produced a harmful effect upon the myocardium.

Therapy

The treatment for hemorrhage is, of course, adequate blood transfusion. Whole blood should be given especially early to those patients in whom a predisposing factor of coronary insufficiency is suspected. Coronary arteriosclerosis, valvular disease, hyperthyroidism, congestive heart failure, and chronic anemia are factors which predispose to the occurrence of acute coronary insufficiency and constitute dangerous potentialities.

Treatment should be instituted before the myocardium is impaired, since in such state intravenous infusion will be to little or no avail.20, 33, 34, 50, 62 The value of the daily electrocardiogram lies in the fact that not only
is it an objective sign of coronary insufficiency but also that it will reveal RS-T depressions and T-wave inversions which may precede the appearance of clinical evidence of coronary insufficiency. Blood should be administered until bleeding has ceased and pulse rate, blood pressures, hemoglobin determinations and electrocardiograms have been restored to normal values.

The treatment of the angina pectoris which appears during hemorrhage is blood replacement.\textsuperscript{74-76} The occurrence of chest pain or the aggravation of pain ordinarily experienced by the patient constitutes an urgent indication for therapy. It is significant that chest pain had appeared in 18 of our patients and in each instance blood transfusion effected either amelioration or disappearance of this complaint. The advisability of repeated transfusions may be questioned in patients with organic heart disease, in view of the possibility of inducing left ventricular failure. Such eventuality is readily admitted. However, we firmly believe that the occurrence of this complication can be prevented, or its severity minimized, even when frequently repeated transfusions are indicated, by careful and slow administration of blood. Constant and studied clinical supervision is imperative.

**Summary**

1. Hemorrhage is one of the most frequent and important precipitating causes of acute coronary insufficiency and assumes grave significance in patients whose coronary circulation is already impaired by antecedent heart disease such as coronary arteriosclerosis, aortic stenosis, enlarged heart. In such patients acute hemorrhage may be followed by myocardial ischemia of sufficient severity and duration to produce clinical, electrocardiographic and anatomic evidence of acute coronary insufficiency.

2. A review has been presented of 103 cases of acute, moderate and severe hemorrhage with references to the amount of rapidity of hemorrhage, blood hemoglobin level, heart rate, blood pressure, presence of shock and electrocardiographic changes. The gastrointestinal tract was the source of bleeding in 85 cases. Fifty-nine cases (57 per cent) presented clinical or electrocardiographic evidence of acute coronary insufficiency; of these, 32 showed electrocardiographic changes alone, 6 only clinical findings and 21 had both clinical and electrocardiographic evidence. The age of patients who developed coronary insufficiency ranged from 18 to 79 years.

3. Twenty-two patients succumbed to the effects of hemorrhage; 18 of these presented clinical or electrocardiographic features of acute coronary insufficiency. In 4 of 13 autopsied cases, pathologic examination disclosed subendocardial myocardial necrosis in the absence of recent coronary artery occlusion.

4. Of the 27 patients with clinical evidence of coronary insufficiency, substernal or precordial pain occurred in 15 instances, congestive heart failure in 8, and both together in 3. Precordial pain varied from mild to severe in nature. In 6 instances its association with shock, tachycardia, and fall in blood pressure simulated massive myocardial infarction due to acute coronary artery occlusion. These symptoms and signs were transient and responded rapidly to therapy. This was especially striking in several cases of recurrent hemorrhage in which each bout of hemorrhage precipitated an episode of severe angina pectoris.

5. Significant electrocardiographic changes occurred in 53 patients. These consisted of flat or inverted T waves in 24 instances, RS-T depression in 4 cases, and combined RS-T and T changes in 25 cases. The latter findings represented the severest degree of coronary insufficiency. Although alterations occurred in all leads, Leads I, II and IV were most frequently affected. Reduced coronary blood flow resulting in anoxia, particularly of the subendocardium, was responsible for the RS-T depressions and T-wave inversions.

6. The changes in circulatory dynamics which were found to be associated with coronary insufficiency following hemorrhage include the shock state, tachycardia, drop in blood pressure and decreased blood volume. Although anoxemia due to fall in hemoglobin was important, it was observed that coronary insufficiency occurred in the absence of anemia when the clinical features of shock predomi-
nated. This emphasizes that rapidity of blood loss may be more significant than the actual amount.

7. The morphologic myocardial changes, when present, varied from tinctorial changes, smudginess of myofibrils and focal necrosis to grossly recognizable confluent zones of infarction. The ischemic lesions were usually noted in the subendocardial region of the posterior wall, septum and papillary muscles of the left ventricle. Pericarditis and mural thrombosis were conspicuously absent. Although coronary arteriosclerosis and varying degrees of stenosis of the lumen were often present, acute coronary occlusion was not found.

8. Hemorrhage exerts a deleterious effect upon the myocardium and was responsible for the production of heart failure in 10 per cent of the cases herein reported. By the same mechanism, hemorrhage may intensify the cardiac failure already present.

9. The proper therapy of shock and anemia following acute hemorrhage in essential for prophylaxis and therapy of coronary insufficiency. Blood should be administered promptly and adequately, particularly in patients with predisposing factors of coronary insufficiency.

REFERENCES


8 MASTER, A. M., and JAFFE, H. L.: Coronary insufficiency and myocardial necrosis due to acute hemorrhage. J. Mt. Sinai Hosp. 7: 96, 1940.


CORONARY INSUFFICIENCY DUE TO HEMORRHAGE


Acute Coronary Insufficiency Due to Acute Hemorrhage: An Analysis of One Hundred and Three Cases

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