MYOCARDIAL AND CEREBRAL INFARCTIONS AS POST-OPERATIVE COMPLICATIONS*

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Many of the complications following surgery, previously critical, are now preventable or readily curable as a result of advances in anaesthesia, transfusion, fluid and electrolyte management, and control of infection. Particularly in the geriatric group, where advancing years no longer constitute a bar to major surgery, myocardial infarction and cerebrovascular accidents are too often the causes of post-operative death. These complications, occurring just when recovery after a technically successful operation seemed assured, are erroneously regarded as non-preventable by surgeons, and few recorded studies of surgical patients have been presented (Master *et al.*, 1938; Davis *et al.*, 1951; Wróblewski and LaDue, 1952; Wasserman *et al.*, 1955).

The present study was undertaken to determine the nature, timing, and pattern of the complications relative to the patient's pre-operative status, the magnitude of operative injury, and the stage of his post-operative response in which the complication occurred. As a result, it might be possible to identify predisposing factors, or at least predict those patients in whom such accidents are likely to occur as a part of their response, or failure to respond, to accidental or surgical trauma.

The series consists of 30 patients at Grady Memorial Hospital and the Veterans' Administration Hospital, Atlanta, during 1956-7, who suffered either a myocardial infarction or a cerebrovascular accident within a period of 30 days of operative or accidental trauma. The large number of geriatric patients, particularly in the charity hospital, contributed to the high incidence of such complications.

The criteria for the inclusion of a patient with a myocardial infarct consisted either of a diagnostic electrocardiographic record, confirmed by a gradual return towards normal, or a positive necropsy finding. Patients without these definite findings were excluded, for the clinical findings in post-operative myocardial infarction are often different from those in the "spontaneous" form of the disease (Menard and Hurxthal, 1931; Jacobs, 1951). Thus cardiac pain is less prominent in the post-operative period, as the patients are often either recovering from general anaesthesia or still under the influence of post-operative analgesics. Unexplained hypotension, tachycardia, arrhythmia, or pulmonary oedema require the electrocardiographic exclusion of myocardial infarction. Infarctions may sometimes go unrecognized; those of minor extent recovering without specific therapy, or coming to light only when a mural thrombus is detached to form a cerebral, peripheral, or pulmonary embolus.

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The criteria for the inclusion of a patient with a cerebrovascular accident were either unequivocal clinical findings, with definite neurological signs such as hemiparesis or hemiplegia, or changes in the brain at necropsy. Lumbar puncture occasionally and electroencephalography rarely were used as adjuncts to diagnosis.

Nineteen patients with myocardial infarcts and 11 with cerebrovascular accidents satisfied these criteria for inclusion.

Material

The average age of the patients with myocardial infarcts was 70 years, of those with cerebrovascular accidents 66 years. The range of ages was similar in both groups: 46-93 years for the cardiac group, 48-80 in the cerebrovascular group. The sex incidence was different in the two groups, being 5 males to 1 female among the cardiacs, 2:1 among the latter group. Of the 19 patients subsequently sustaining a myocardial infarction, 12 (63%) had pre-operative evidence, apart from arteriosclerosis and mild hypertension, of cardiac disability. It is striking that, of the seven whose pre-operative evaluation was negative, three showed evidence of old as well as recent infarction at necropsy, one of these having had a normal electrocardiogram. Of the eight patients with pre-operative electrocardiograms, only three showed an abnormality indicating ischaemia. Two of these three patients developed post-operative myocardial infarcts; the other had a cerebrovascular accident.

The patients with cerebral complications showed a rather similar picture. Pre-operatively, five (45%) had evidence of cardiovascular disease apart from mild hypertension. One of the six without pre-operative evidence of cardiovascular disease had clear evidence at necropsy of both old and recent areas of cerebral softening.

Hypertension (systolic pressure over 140 mm. Hg. or a diastolic pressure over 90 mm.) was present in 19 (63%) of the 30 patients.

In retrospect, two-thirds of these patients might have been expected, on estimation of their pre-operative cardiovascular status, to have a predilection for one of these complications. However, in attempting to make a total appraisal of each patient, taking into account not only his cardiovascular reserve but also the magnitude of the anticipated surgery, only 7 out of the 30 patients were classified as relatively "good risks" from the point of view of fitness for anaesthesia and surgery.

Operation and Injury

Among the patients who developed myocardial infarction the site of operation or trauma was the abdomen in 11 patients, the extremities in 5, and the chest in 3. In the cerebrovascular group the abdomen was the site in 6, the extremities in 2, the chest in 2, and the neck in 1. Thus operations on the abdomen preceded these complications in half of the patients. Those with cardiac or intracranial operations were excluded.

Nine of the myocardial infarcts were preceded by accidental trauma or emergency operations and 10 by elective procedures; five of the cerebral accidents were preceded by emergency and six by elective procedures. The complications, therefore, were equally divided between the urgent and elective operations or, stated differently, between the acute and chronic diseases.

The type of anaesthesia varied. The most striking feature in a detailed analysis of the agents used is that the complications followed the use of local analgesia in seven patients (23%). Of the 13 which followed general anaesthesia, relaxant agents were used in seven. Spinal anaesthesia was used in six patients, refrigeration in one, and no anaesthetic was given to three (two burns and one fractured humerus). The two complications showed approximately equal distribution of the various anaesthetic agents.

Shock and Hypotension

No patient was hypotensive pre-operatively. Nine (47%) of those with myocardial infarcts had a recognized period of hypotension during operation or anaesthesia, but in two of these the infarction was so closely related to the hypotensive episode that the latter might have been effect rather than cause. In several patients the sequence of events appeared clearly to indicate that the infarction occurred during a period of surgically induced hypotension, the hypotension causing the infarction. The following case-history is illustrative:

A 68-year-old man was assessed before resection of an aneurysm of the abdominal aorta. He was arteriosclerotic, with early fundal changes; his blood pressure was 165/90 and the pulses in his right lower extremity were diminished. He was anaesthetized with thiampyl sodium, nitrous oxide, oxygen, and suxamethonium chloride. The aneurysm was resected and a graft inserted without untoward effect. Removal of the aortic clamps produced a profound fall in blood pressure, which did not respond to adequate blood replacement and necessitated intravenous L-noradrenaline for the ensuing seven days. An electrocardiogram taken in the operating-room following the hypotensive episode revealed an acute myocardial infarction. He made a full recovery.

There was a period of hypotension during or after operation in seven (64%) of the patients who later had cerebrovascular accidents.

A known period of hypotension preceded at least one-third of the myocardial infarcts and two-thirds of the cerebrovascular accidents.

Time of Complication after Surgery.—The times of onset of the two complications showed a significant difference. Twelve of the 19 (63%) myocardial infarcts occurred on the day of operation or within the first three post-operative days; only 3 of the 11 (27%) cerebrovascular accidents did so, the remainder being spread over a period of the ensuing three post-operative weeks. Several of the latter accidents occurred at the beginning of the second week, the period often associated with a high incidence of thrombo-embolism in the venous system. In general, the patients in this series had cerebral accidents at any time throughout the first three weeks after operation or trauma, whereas myocardial infarction rarely occurred after the end of the first week.

Discussion

The finding that myocardial infarction occurred predominantly in older men agrees with findings in other series, apart from that of Wasserman *et al.* (1955), who had only 10 men in their group of 25 patients. The general incidence of myocardial infarction, unrelated to trauma, shows an average age of 62 years and a proportion of females varying from 7 to 17% (Bland and White, 1941). The various post-operative series show an average age of 62–69 years and the rather higher proportion of females of 16–60%.

Pre-operatively, two-thirds of the patients in this study had definite clinical manifestations of cardiovascular disease. The difficulties of adequate evaluation are apparent, however, from the presence at necropsy of old cerebral and myocardial infarcts which were unsuspected from the history, physical examination, and electrocardiogram. Master *et al.* (1938) found pre-operative evidence of cardiovascular disease in almost every one of his 35 patients.

The nature of the surgical procedure and the type of anaesthesia had little bearing on the incidence of complications. Apart from the dangers of hypotension in spinal anaesthesia (Davis *et al.*, 1951; Wasserman *et al.*, 1955) the lack of anaesthesia in three patients, local analgesia in seven, and refrigeration in one suggest that these complications do not result from the use of any specific anaesthetic agent. No known anaesthetic agent affects directly the oxygen-carrying capacity of the blood (Adriani, 1955).

The pathogenesis of myocardial infarction is obscure, but the actual lesion may take several forms. When the coronary arteries are already atherosclerotic a small thrombus may form on an atheromatous plaque or an intimal

haematoma may occlude the lumen, infarction occurring if the patient survives long enough for the myocardial degeneration to follow. It is also now recognized that infarction may follow a period of diminished flow (coronary insufficiency), without demonstrable occlusion of the arterial lumen, when there has been a discrepancy between the demands of the myocardium and the available blood supply (Master *et al.*, 1947).

Such a discrepancy may follow an increase in the oxygen requirements of the myocardium as the cardiac work suddenly increases to meet the demands of an increase in blood pressure, cardiac rate, or cardiac output. This may result from severe physical exertion, emotional stress, tachycardia from any cause, or after the administration of such drugs as adrenaline. A similar discrepancy follows a sudden diminution in coronary flow as a result of hypotension, oligoemia, or extreme bradycardia. In a study (Vowles *et al.*, 1957) of coronary flow in dogs, coronary sinus flow was found to fall by 50% in acute haemorrhagic shock, despite a lowered coronary vascular resistance (Fig. 1). In

FIG. 1.—Coronary sinus flow and vascular resistance in shock (Vowles *et al.*, 1957).

the presence of coronary arteriosclerosis, vasodilatation may be so limited that haemorrhagic shock may result in an even more profound decrease in coronary flow. The haemodynamic law of Poiseuille, which states that if the pressure remains constant the flow in a tube varies as the fourth power of the diameter, emphasizes the great reduction in flow which occurs in a vessel narrowed by arteriosclerosis to half its normal diameter; if the systolic blood pressure falls only from 120 to 90 mm. the flow is $\frac{1}{16} \times \frac{1}{4}$ —that is, under 5% of normal. A fall from 120 to 30 mm. reduces the flow in such a vessel to 2% of normal (Fig. 2).

FIG. 2.—Diagrammatic representation of blood flow at normal blood pressure and in shock, in normal coronary vessels, and in vessels narrowed by arteriosclerosis to half their normal diameter. A, Normal flow. B, Flow = normal flow $\times \frac{1}{2} = 6\%$. C, Flow = normal flow $\times \frac{1}{4}$ (fall in pressure) $\times 2$ (diminished resistance) = 50%. D, Flow = normal flow $\times \frac{1}{4} \times \frac{1}{2} = 2\%$.

In the current series a known period of hypotension preceded a significant number of the myocardial infarctions. Impairment of oxygenation of the coronary blood in anaemia or anoxia from respiratory depression or pulmonary dysfunction will result in a similar deficit. Many of these factors may be present in patients submitted to anaesthesia and major surgery, and in view of the large number with coronary artery disease it is surprising how few infarcts actually occur.

Phipps (1936), reviewing 437 cases of acute myocardial infarcts, found that 6% followed surgery, 13% followed a period of unusually severe exercise, 18% followed moderate or usual exercise, 51% occurred at rest, and 8% occurred during sleep. The high proportion of infarcts occurring in patients at rest was confirmed by Master *et al.* (1937), who found that 52% of 815 infarcts (in 555 patients) occurred

with the patient at rest. Master *et al.* pointed out, however, that these percentages correspond with the proportion of time spent in these various activities, and regarded them as insignificant. On the other hand, Fitzhugh and Hamilton (1933) found that in a high proportion of his patients the acute incident followed a period of unusual effort often accompanied by undue fatigue, inadequate sleep, and emotional strain. Some of these less easily assessable factors may well play a part in patients undergoing surgery. The occurrence of myocardial infarction following hypotension due to haemorrhage, "pleural shock," pulmonary embolism, or peritonitis has been described (Davis *et al.*, 1951).

Cerebrovascular "accidents" are usually classified into haemorrhage, embolism, thrombosis, and spasm. Hicks and Warren (1951), in a study of 100 necropsies of patients dying of these accidents, regard this classification as misleading. They believe that many of the haemorrhages demonstrated at necropsy are due to coalescence of minute petechiae into an infarcted and necrotic area, ischaemia being the underlying cause of all except the embolic lesion. In 60% of their necropsies showing infarction there was no vascular occlusion. They suggest that arterial spasm, which may respond to stellate ganglion block (Leriche and Fontaine, 1936) is the cause of hypertensive encephalopathy. Sodium and water retention, with cerebral oedema, small-vessel compression, and resultant ischaemia, may play a part similar to the mechanism underlying the encephalopathy which sometimes follows the administration of corticotrophin and cortisone (Josiah Macy Jr. Foundation, 1949).

In recent years the physiology of cerebral blood flow has been advanced by the nitrous-oxide desaturation technique of Kety and Schmidt (1948). Provided that the blood pressure remains above 60 mm. systolic, cerebral vasodilatation maintains adequate flow. Anoxia, carbon dioxide, ether, histamine, papaverine, and a local increase in metabolic needs due to cerebral activity are potent vasodilators. L-Noradrenaline is a cerebral vasoconstrictor in the normotensive patient, oxygenation being maintained by increased oxygen extraction. In the hypotensive patient noradrenaline still results in vasoconstriction, but the flow is so increased by the rise in pressure that oxygenation is improved. Anxiety and apprehension cause an increased oxygen consumption, but under general anaesthesia oxygen consumption is lowered to 40% of normal, normal flow being maintained (Kety and Schmidt, 1948; Kety, 1950).

In patients over 50, even though symptom-free, there is a reduction in cerebral blood flow and an increased vascular resistance compared with the younger age groups. These changes, which are even more marked in those with a history of cerebrovascular accident or evidence of arteriosclerotic psychosis, are not reversed by inhalation of oxygen, but are restored almost to normal by 5% carbon dioxide (Fazekas *et al.*, 1952; *Lancet*, 1954; Saunders, 1954).

Even without this apparent state of chronic spasm an acute form of cerebral vascular insufficiency may arise during hypotension from haemorrhage, coronary occlusion, spinal anaesthesia, or even sudden postural change. This generally transient and reversible insufficiency may produce irreversible damage to the brain. In monkeys, when one carotid or other large cerebral vessel has been experimentally occluded without detectable effect, induced hypotension then has a focal effect such as hemiplegia, from which the animal recovers if the hypotension is sufficiently transient. (Corday *et al.*, 1953).

Cerebrovascular accidents have been recorded after minor surgery, diagnostic procedures, and minimal accidental trauma, indicating that there are other more obscure factors of importance (Hammes, 1956).

It is apparent that several factors are common to the two post-operative complications. The hypertensive arteriosclerotic patient has a decrease in vascular adaptability with regard to these vital organs; an acute state of insufficiency occurs if there is a fall in pressure, a local increase in

vascular resistance, diminished oxygen-carrying capacity of the blood, or an increased local metabolic demand. If the insufficiency is due to an actual vascular occlusion, ischaemia and infarction follow in heart muscle or brain. Even if the insufficiency is transient, irreversible changes may result. In this respect myocardial cells are less sensitive than cerebral cells; the latter can survive only four to five minutes of complete anoxia, those of the higher centres dying first. On the other hand, myocardial infarction may cause the immediate death of the patient, a sequence which rarely happens with cerebrovascular ischaemia.

Although the two complications have several antecedent factors in common, they present a striking difference in their time of occurrence, two-thirds of the myocardial infarctions being on the day of operation or the succeeding three days. Similar data are reported by other observers (see Table).

Time of Onset of Post-operative Myocardial Infarcts.

Author	Total No. of Patients	Percentage of Infarcts Occurring on Day of Operation and First Three Post-operative Days	Percentage of Infarcts Occurring During First Post-operative Week
*Davis <i>et al.</i> (1951)	18	83	89
Wróblewski and LaDus (1952)	15	60	66
Wasserman <i>et al.</i> (1955)	25	68	92
Master <i>et al.</i> (1938)	35	52	63
Current series	19	63	76
Total	112	65	77

* These patients are reported according to day of death.

The cerebral accidents were spread out over the first three post-operative weeks (Fig. 3). During and after trauma or operation, the factors operating to cause diminished oxygenation and hypotension are identical, but the metabolic demands of the heart and brain are not. Myocardial infarction is a result of a discrepancy between the needs and the available supply of oxygen to the myocardium. This discrepancy is most likely to arise during or immediately after the anaesthesia, and accidental or operative trauma;

for at this time myocardial irritability is often increased, while tachycardia, hypotension, diminished venous return, peripheral circulatory changes, and alterations in depth and rate of respiration may all increase cardiac work and oxygen demands (Fig. 4). Once this period of maximal cardiovascular stress is over, it is unlikely to recur except as a result of a major mishap such as post-operative haemorrhage.

FIG. 3.—Incidence of myocardial and cerebral infarctions in successive post-operative weeks.

FIG. 4.—Incidence of myocardial infarctions on successive post-operative days.

Cerebral infarction is similarly due to a discrepancy between cerebral supply and demand for oxygen. Under adequate general anaesthesia, oxygen demands of the brain are so reduced (to less than half their normal value), that, unless gross anoxia such as that due to delay in treatment of cardiac arrest occurs, the oxygen supply is likely to be adequate. The brain is in a relatively protected state. Of the three patients in the current series whose cerebral infarcts occurred in the first week (on the day of operation and the first post-operative day), two had operations under local and one under spinal anaesthesia, so that this protection was lacking. Later in the post-operative course, continued narcotic administration, without the artificially augmented respiration of the operating-room, may cause respiratory depression and cerebral anoxia. Unfortunately it is the garrulous and wakeful patient with cerebral arteriosclerosis and a reversal of the normal sleep rhythm who is particularly likely to receive heavy nocturnal sedation. The high incidence of cerebrovascular accidents after cataract surgery and skeletal trauma is well known. The balance between the supply and demand of cerebral oxygen is so delicate that only a minor further mishap is needed to tip the scales. Anoxia follows, and need only be unrelieved for five minutes for the cerebral damage to be permanent.

Summary

A review of 30 patients who experienced cardiac or cerebral infarction during the 30 days following operation or accidental trauma suggests a biological difference between these two processes. Of the cardiac infarctions, 63% occurred during the operation or within the first three days after operation or injury. All but 23% occurred within the first week. To the contrary, the cerebrovascular accidents occurred without apparent predilection of time.

A period of hypotension was known to be associated with operation in 53% of the patients. Hypotension is known to result in a reduction in coronary flow. In the arteriosclerotic patient, whose coronary arteries are unable to dilate appreciably, the reduction in flow following hypotension is probably a major factor in the progression of ischaemia.

The complications could not be related to the anaesthetic agents used; indeed, eight followed the use of local analgesia. One patient received no anaesthesia (fractured humerus).

The increased oxygen requirements of the burdened heart, associated with the decreased coronary flow of hypotension, predispose it to an immediate oxygen deficiency. General anaesthesia reduces the oxygen demands of the brain so that an absolute oxygen deficit is as likely to be post-operative (atelectasis, narcotic respiratory depression, postural changes) as operative.

An urgent need is the rejection of the surgeon's concept that most of these complications are inevitable. Application and extension of the recognized principles of avoidance of anoxia, hypotension, and increased cardiac work in arteriosclerotic patients should prevent many of the myocardial infarctions. The biological and clinical factors underlying cerebrovascular accidents differ in not being specifically related to the period of trauma; attempted prevention necessitates the empirical application of such measures as adequate oxygenation, inhalation of carbon dioxide, and the avoidance of undue sedation in arteriosclerotic patients.

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TRENCH-FOOT IN PEACETIME ENGLAND

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Severe injury from cold is seen in three main forms. Frostbite occurs if the temperature is low enough to cause actual freezing of tissues, while more prolonged exposure to a cold but non-freezing environment results in a trench-foot type of injury. Although this derives its name from its prevalence during the trench warfare of 1914–18, the occurrence of trench-foot among Napoleon's troops during the retreat from Moscow was described by Larrey (1812), and practically every military campaign fought in cold climates since that time has produced further cases. Similar to trench-foot in many respects is immersion foot, numerous examples of which were observed among shipwreck survivors in the 1939–45 war (Ungley and Blackwood, 1942; Webster, Woolhouse, and Johnston, 1942; White, 1943), while it has been suggested (Greene, 1941) that shelter foot is another type of local cold injury. It seems possible, however, that mechanical obstruction to the venous return, coupled with some deficiency of vitamin C, is more important than cold in the production of this last-named condition. Frostbite is a result of cold which may occur in time of war or peace (Brahdy, 1935; Kleitsch and Connors, 1954; Butler, 1957). Prolonged exposure to a low but non-freezing temperature is, however, very unlikely to occur under normal conditions of peace, and trench-foot is primarily a hazard of war.

The occurrence of two cases in peacetime England is rare enough to warrant this report. We have, in fact, been unable to find any record of similar cases occurring in this country, although the circumstances under which our patients sustained their injuries cannot be unique.

Case 1

A vagrant aged 54 first took to the roads in 1937. Apart from service with the Army from 1939 to 1945 he had had nothing but casual employment during that time, and had