SOME PHYSIOLOGICAL FACTORS AFFECTING OPERATIVE RISK*

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IT IS not the purpose of this presentation to go into the multitudinous factors which determine operative risk; in particular, no attempt will be made to assess the dangers of various anaesthetic agents and methods. Such would be the height of temerity on the part of a physician addressing an audience of anaesthetists. Rather, it is its purpose to consider the results of the stress of an anaesthetic and an operation on the patient and how such stress can affect various vital organs and so to some extent determine the risks involved.

Francis Moore[1] has expressed the view that the term "operative risk" should be abandoned—that one is really only determining what course is best for the patient. Yet this is surely a matter of semantics. Whether or not the term "operative risk" is employed, the doctor must weigh the good to be gained against the danger to the patient of the therapy employed. There is hardly any therapy that can be recommended that does not present some possible danger to the patient. It might merely be mentioned that the commonplace aspirin tablet may cause gastritis from which serious haemorrhage may arise.

This presentation then will consider the dangers to the patient accruing from three major stresses provided in greater or lesser degree by operation under general anaesthesia: reduction in blood volume through blood loss, hypoxia, and adrenal cortical stimulation.

Decrease in circulating blood volume, now usually controlled by transfusion of whole blood or blood substitutes, results in diminished cardiac filling, diminished output per beat, diminished systolic and mean blood pressure, and hence diminished flow to vital organs. The stimulation of stretch receptors of the juxtaglomerular apparatus and others whose exact site is uncertain, but some of which are possibly situated in all the chambers of the heart, causes an increased secretion of aldosterone by the adrenal cortex. This results in increased absorption of sodium and decreased absorption of potassium by the distal convoluted tubule of the kidney.

The secretion of antidiuretic hormone (A.D.H.) by the posterior pituitary results from stimulation of stretch receptors of uncertain location, from tissue damage, from visceral manipulation, and, of great importance, from stimulation of osmoreceptors in the hypothalamus. The latter is the result of the retention of sodium by the aldosterone effect previously described. The increased secretion of A.D.H. results in increased reabsorption of water by the distal convoluted tubule. Thus a whole salt- and water-retaining mechanism is set in motion.

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It is of interest to consider how deceptive clinical evaluation of blood loss and changes in blood volume may be. During the Battle for Rome, No. 15 Canadian General Hospital was at once the forward and the base hospital at the beginning of the action. The hospital had the good fortune to have attached No. 1 Canadian Mobile Research Unit—affectionately known as the "Mobile Brains." Dr. Robert Cleghorn—now a highly esteemed psychiatrist—was very much interested in shock. It became evident from the observations of blood volume determined by Cleghorn and his colleagues that at a time when a seriously wounded man was deemed fit for operation by the crude criteria of clinical state, blood pressure, and pulse, he was still about 1000 c.c. short of his calculated normal blood volume. The policy was then adopted of giving a further litre of blood when the patient was considered fit.

Today there are better methods available than the Evans blue used by Cleghorn. Using tracer isotopes, blood volume can be determined at the bedside or on the operating room table in ten to thirty minutes. The use of such methods will in the near future aid in further reducing the present imponderables that contribute to operative risk.

One may ask why such lesser reduction in blood volume should cause concern. Some, including Peretz, Dossetor, and McGregor[2] in Montreal, have produced evidence to indicate that before there is hypotension from blood loss there is decreased regional blood flow that produces anoxia and, with anoxic metabolism, increased production of lactic acid. Such lactic acidosis will potentiate the adverse effects of hypoxia to be described later.

One of the problems of shock due to blood loss is the use of vasopressor substances in its treatment. Some physicians feel that norepinephrine or similar vasoconstricting drugs should always be used. Others feel that such drugs do more harm than good, in that the arteriolar vasoconstriction which raises blood pressure at the same time reduces regional flow. This group prefer treatment by sympathetic ganglion blocking agents which, by dilating the arterioles, permit adequate perfusion at lower pressure. Possibly both groups are right in certain circumstances. If the extremities are pale and cold, indicating vasoconstriction, surely little is to be gained by vasconstricting drugs, and the second approach is more likely to be helpful. If, however, the extremities are warm, and particularly if the arm veins are full, then norepinephrine will be most helpful, not only by increasing arteriolar tone and so raising diastolic and mean blood pressure, but also by causing venoconstriction. It must be remembered that about 75 per cent of the blood volume is in the veins (20% arteries, 5% capillaries) and that venoconstriction by increasing venous pressure and hence venous return will increase cardiac output. Such treatment must be exhibited with care lest the increased venous return be so great as to precipitate pulmonary oedema.

Hypoxia, fortunately a rare event with modern anaesthesia, may have far-reaching effects. It gives rise to increased tone of the pulmonary arterioles, pulmonary hypertension, and increased load on the right ventricle. If hypoxia is combined with carbon dioxide retention, the effect on pulmonary arterioles is potentiated, whereas the systemic arterioles are dilated, causing reduced peripheral resistance, increased filling of the right atrium, and increased cardiac

output. It is thus possible to find a high output state combined with pulmonary hypertension. The high output state can be recognized by elevation of systolic blood pressure with low diastolic pressure and hence wide pulse pressure, warm, pink extremities, increased digital throb, capillary pulsation, full arm veins, and an active left ventricle. It is to be noted that with normal heart and lungs these changes are minimal and cause no trouble at all unless the hypoxia is of very serious degree. The burden of hypoxia falls heavily on the heart and brain for reasons which will be discussed later. As mentioned before, the effects of hypoxia are accentuated by lactic acidosis due to hypovolemia.

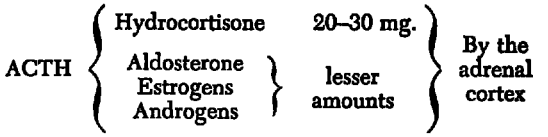
Adrenal cortical stimulation has wide-spread effects resulting from increased output of adrenal corticosteroids. Increase in mineralo-corticoids results in retention of sodium and loss of potassium, as previously described. In the main, this effect is advantageous to the organism. Were it not for this response to injury, a wounded animal would be in a sorry plight if it could not find a pool of water and a salt lick. It is only when the doctor, ignorant of these effects, administers salt and water too liberally or omits to provide adequate potassium that this reaction to injury becomes dangerous.

In the days before the flame photometer, when the determination of serum potassium by the chemical method took two days, few people were aware of the hazards of potassium depletion. Patients receiving the best postoperative care were carefully hydrated, given glucose and saline intravenously—but no potassium. This very treatment tended to augment the mineralo-corticoid effect insofar as potassium loss was concerned.

It is of historic interest to recall that the physicians of fifty years ago put great faith in the use of beef juice in the postoperative period. Subsequently, its use was abandoned when it was shown that beef juice contained virtually no protein or calories. It is, however, rich in minerals. Perhaps our forebears were wiser than we.

On the contrary, the failure of the pituitary-adrenal axis to function properly, as seen in patients whose adrenal cortical activity is suppressed either by Addison's disease, Simmonds' disease, or the prolonged administration of cortisone, is well known as a major hazard to the stress of surgery which can be countered only by replacement of the missing hormones.

The function of the pituitary adrenal axis can be very simply expressed in the following diagram:



Today, by using the ACTH stimulation test, S.U. 4885, and serum cortisol levels, the functional state of the axis can be very precisely assessed.

It is now desirable to consider the effect of the physiological factors described on the function of the vital organs—heart, brain, kidney, and liver—both when healthy and when diseased.

The heart is dependent for its blood supply very largely on coronary flow. In the normal resting state, the blood in the coronary sinus is only 30 per cent saturated with oxygen. This is to be compared with the 60 per cent saturation of venous blood leaving other organs. Since at this level of oxygen saturation, haemoglobin releases very little more, it is evident that the only way increased oxygen can be supplied to the heart is by increased coronary flow. The effects of diminished blood volume with lowered mean blood pressure and hence decreased coronary flow will be readily appreciated. If to this is added hypoxia, the arterial oxygen saturation will be reduced and the resultant increase in tone of the pulmonary arterioles causes pulmonary hypertension, with increased work for the right ventricle. If to this again hypercarbia is added, the pulmonary hypertension is increased, whereas the systemic arterioles are dilated and the high output state so produced increases the work of both ventricles, particularly the left. The right ventricle handles increased volume well, but is a poor force pump, and hence easily embarrassed by pulmonary hypertension.

The stress provided to a normal heart is not great unless lung disease has potentiated the changes. But if to this is added coronary atherosclerosis or valvular heart disease of a type which reduces the mean arterial blood pressure—notably aortic or mitral stenosis—then the hazards are increased, as the ability to increase the oxygen supply to the heart by increased coronary flow is greatly reduced and the muscular hypertrophy accompanying such valvular disease further increases the demand for increased blood flow. The results are well known—there is an increased risk of cardiac arrest or dangerous cardiac arrhythmias.

The presence of recent myocardial infarction, by producing an irritable myocardium, greatly increases the risk of arrhythmia and arrest and constitutes a contraindication to all but emergency, life-saving operative procedures.

Heart failure, by aggravating all the disturbances mentioned, constitutes a similar contraindication.

Two factors render the brain particularly susceptible to injury by ischaemia. In the first place, nerve cells are dependent for life upon glucose and oxygen. Deficiency of either lasting for more than a few minutes results in irreversible injury. The evidence of such deficiency that can be seen on microscopic examination of brain tissue in fatal cases is vasodilatation, oedema, and petechial haemorrhage. Sometimes the evident damage appears too trivial to have caused death. To understand the far-reaching effects of cerebral oedema, the second factor must be considered. The brain, unlike other organs, lies within a rigid box, the skull. Semifluid in consistency, the brain has at least one physical property of fluid—it is incompressible. If oedema occurs, room must be made inside the skull. The only way which space can be quickly provided is by compression of the veins and venous sinuses, thus squeezing blood from within the skull. Such compression, however, will embarrass the cerebral circulation and aggravate the oedema.

For these reasons physicians face with apprehension necessary surgery for patients with evidence of impaired cerebral circulation. They also provide the necessity for carefully assessing the cerebral circulation in older patients facing such stress. This requires a careful inquiry regarding the occurrence of a

previous cerebral vascular accident or of "little strokes." In the presence of such a history only life-saving surgery should be undertaken.

When no such history is obtained the cerebral circulation can be further assessed by bedside examination. The retina is a projection of the brain and its vessels reflect accurately the state of the cerebral vessels. Careful ophthalmoscopic examination of the retinal vessels is then an imperative part of the preoperative examination of a patient.

It is equally important to gain as much knowledge as possible of the state of the arteries entering the skull. Differences in pulsation are sometimes helpful, but the most valuable evidence of atherosclerosis of the carotids is the presence of a bruit. This must be distinguished from a venous hum by the simple manoeuvre of compressing the jugular vein below the angle of the jaw. While evidence of atherosclerosis in similar sized vessels elsewhere may arouse suspicion, it does not of necessity indicate that the carotids or vertebrals are involved.

The physiological disturbances resulting from operative stress are well tolerated by the healthy brain. Normally the venous blood leaving the skull is still 60 per cent saturated with oxygen, and decreased cerebral circulation can be compensated to a considerable degree by this reserve supply.

The role of arterial P_{CO_2}, the most important controlling influence in central blood flow, is well known to anaesthetists and will not be considered further.

If the blood supply to a portion of the brain is compromised by atherosclerosis of the cerebral vessels or of the carotid-vertebral system, the danger of serious ischaemia is greatly enhanced. The results are well known—death or serious brain damage can result, and the need for careful anaesthesia and a "good operation" are evident.

The kidneys almost always reflect the stress of operation to some degree by a period of oliguria lasting usually 24 hours or less. The reason for such oliguria is provided by the two factors of reduced blood volume and consequent lowered renal flow and lowered glomerular filtration rate, together with the A.D.H.-aldosterone mechanism previously described, and by the direct stimulation of the pituitary adrenal axis by the operative stress.

Although the kidneys reflect accurately the stress of operation, lasting or serious damage is fortunately rare. However, the persistance and aggravation of the above mechanisms can result in anuria and acute renal failure. In patients with previous damage to the kidneys by urinary obstruction, pyelonephritis, or Bright's disease the risk is greater. This has long been recognized by the urologists, who take pains to relieve the functional disturbance as far as possible before undertaking definitive surgery.

The liver as a source of danger from the stress of operation is seldom considered important except in operations on the biliary tract, or in porto-systemic venous anastomosis for the treatment of oesophageal varices. Perhaps the double blood supply of the liver provides some protection. Certainly it is true that when the liver is damaged the stress of operation becomes quite apparent.

Various means have been employed to assess the suitability of patients to undergo porto-caval shunt. The most popular demands the addition of a battery of liver function tests to the clinical assessment of the patient. Unfortunately, as

Linton[3] has reported, 49 per cent of patients admitted with haemorrhage from oesophageal varices due to portal cirrhosis die before such assessment can be completed. In Halifax, an attempt is being made to assess the patient's fitness for operation at the bedside in the belief that recent haemorrhage, by further embarrassing the hepatic circulation and giving a high protein meal, has provided a better test than any other available. It is well known that high protein intake and shock are two of the most important precipitating causes of hepatic failure with coma: the latter, by further compromising hepatic function through diminished blood supply; the former, by increasing the production of ammonia in the gut. Thus the acute episode of haemorrhage has combined both these stresses into one built-in test. All one need do is read the result. If the patient when examined after an acute episode of bleeding shows no mental confusion or drowsiness, is free from flapping tremor, and has reasonably good muscular co-ordination as indicated by legible handwriting, it is likely that he will tolerate a porto-caval shunt.

Nevertheless, the operation may precipitate hepatic failure, which must be treated with intelligence and vigour. That such an event is reversible is illustrated by a patient who in 1957 underwent splenectomy and splenic renal anastomosis, indicated by portal hypertension due to hepatic cirrhosis with congestive splenomegally and severe hypersplenism, together with oesophageal varices which had never bled. He developed hepatic coma in the postoperative period and was very ill for two weeks. He is alive, well, and enjoying life today, eight years later.

Some reference should be made to the controversial hepato-renal syndrome. Following operations involving the biliary tract, particularly where there has been prolonged obstruction of the common bile duct, in very rare instances the patient develops acute renal failure, deepening jaundice, and other signs of hepatic failure, and lapses into coma and dies. Some believe this to be a specific disorder. Others, including the writer, believe that it represents the combined effect of the stress of operation on the two organs mentioned, combined with electrolyte disturbance and sometimes other complications within the abdomen. The relief of prolonged obstruction of the common bile duct is virtually always followed by a period of deepening jaundice before recovery sets in. It would appear that decompression of the biliary tract exerts an unfavourable though fortunately temporary effect on hepatic function. This, combined with the effects on kidney function, appears to account for the findings.

In conclusion, one must say, and say with gratitude, that the advances in anaesthesia over the past 25 years have resulted in so much safer surgery that it rather tends to be taken for granted. It is only by sober reflection on matters such as have been presented in this paper that the magnitude of the contribution of anaesthesiology to medical progress is appreciated.

REFERENCES

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