

A METHOD OF REDUCING THE INCIDENCE OF FATAL POSTOPERATIVE PULMONARY EMBOLISM

RESULTS OF ITS USE IN FOUR THOUSAND FIVE HUNDRED SURGICAL CASES¹

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CLINICAL investigation has been, and should continue to be, a reliable method of securing information. We have but to review the work of Richard Bright on nephritis, that of Addison on tuberculosis of the suprarenal glands and on pernicious anæmia, and the many recent advances in medicine developed by deduction from clinical observations substantiated by postmortem reports to appreciate the value of clinical investigation. Experimental investigation and research leading to deductions referable to clinical problems have so well justified themselves that unless deductions made from clinical investigation are proved to be facts by animal experimentation we may look on the results of such work as suggestive but not proved. Pulmonary embolism is one of the great surgical problems. Unfortunately, up to the present time, it has been difficult to produce pulmonary emboli experimentally in a manner which simulates their formation in human beings. In more than 60 experiments on animals, Miller and Rogers were unable to produce pulmonary emboli that might be compared in formation and condition to emboli in human beings. The deductions which I am making in the presentation of this material are essentially the result of clinical investigation. Yet these investigations carried on over a period of 4½ years in a large group of cases have proved of great clinical value.

Many physiological changes and adjustments follow surgical procedures. Those seemingly concerned in the formation of postoperative pulmonary emboli are: (1) decrease in metabolic activities; (2) the tendency toward a decrease in the rate of blood flow (pointed out by Virchow in 1846) with a decrease in blood pressure; and (3) changes in the cellular constituents of the blood.

These conditions may be the result of: (1) rest in bed without food; (2) interference with

circulation by intra-abdominal manipulation; (3) forty-eight hours of intestinal quiet after intra-abdominal operations; and (4) muscular splinting of the abdominal wall because of a painful incision.

Any method which would cause an increase in metabolism, in rate of the flow of blood, and in blood pressure should decrease the incidence of fatal postoperative embolism. The embolism can be increased effectually by the use of desiccated thyroid gland. Clinical support of the value of increased metabolism in the prevention of thrombosis and embolism is lent by Plummer's observation that in cases in which the thyroid gland is hyperfunctioning, thrombosis and embolism practically never occur even when disturbances of blood flow are extreme from associated cardiac decompensation. In contrast to this is the frequent association of thrombosis and often fatal embolism in patients with primary cardiac decompensation. When 1 milligram of thyroxine was administered daily for 3 days to rabbits by Shionoya and Rowntree, thrombosis did not occur for from 25 to 30 minutes, in contrast to thrombosis occurring in their control animals in from 4 to 10 minutes. This change in blood flow and the late formation of the thrombosis following thyroxine experimentally administered by them was sustained for 3 days.

The tragic deaths from pulmonary embolism are those occurring in patients who, except for the lesion for which they are being operated on, are in good condition. Most of the reported deaths from fatal pulmonary embolism have occurred in patients of this type, yet death did not occur among patients of this type in the series of 4,500 surgical cases in which the method of prevention which I am presenting was used. Any method of reducing the incidence of postoperative pulmonary embolism should have its greatest possibility in this group of cases. Attention, therefore, is

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directed to the fact that in contrast to success of the regimen among patients who are in good condition, experience seems to show that cardiovascular disease or diseases of other parenchymatous organs which debilitate or weaken the patients predisposes to the formation of thrombi and emboli. One of the most important factors concerned probably in their production is the change in blood flow occurring simultaneously with decompensation of the function of these structures.

In the statistical review by Henderson of 113 cases of pulmonary embolism in The Mayo Clinic during the 10-year period from 1917 to 1927, there were 46 non-surgical cases in which fatal embolism occurred. Half of these patients had myocardial degeneration with marked decompensation. In some of the non-surgical cases, pulmonary emboli were found unexpectedly at necropsy, when death had appeared to be due to cardiac failure from myocardial degeneration, peritonitis, bronchitis, or hæmorrhage, and embolism had come into the picture as a terminal event.

Kuhn, at the Institute of Pathology at Freiburg, recently reported that the incidence of fatal embolism in Germany from 1924 to 1927 increased from 1.3 to 4.9 per cent, whereas in 1927 thrombosis was found in every fourth body examined, and fatal embolism was found in every twentieth body. He stated his belief that this increase in the incidence of thrombosis and embolism is the result of prolonging life by the treatment of patients with chronic disease of the heart. With such disease, changes in the flow of blood occur.

Further evidence of the tendency to the formation of thrombi and emboli in patients who are debilitated by disease is found in the fact that the incidence of fatal postoperative embolism was three times greater after cystostomy preliminary to prostatectomy on debilitated patients than after the same operation performed on patients in good condition. The effect of cardiovascular disease and disease of the parenchymatous organs as the predisposing and probably uncontrollable factor of pulmonary embolism has been emphasized because of the problem of compensating for these fixed pathological changes and because it emphasizes the influence of changes in

the flow of blood in the formation of such emboli.

In the series of 4,500 surgical cases which I am reporting, pulmonary emboli were found at necropsy in 4 cases; 3 of the patients were more than 70 years of age and had advanced cardiac disease. In 2 cases pulmonary emboli were found unexpectedly at postmortem examination; death was the result of uræmia in 1 case and of sepsis in the other. The other patient, a woman aged 54 years, had auricular fibrillation, and died on the sixth day following her operation. She had received only 4 grains of desiccated thyroid gland the preceding day.

Since mention has been made of the predisposition of elderly patients with debilitating disease to the formation of thrombi and emboli, especially in cases of cystostomy as a preliminary to prostatectomy, it is of interest that in this series of operations 779 were performed on the prostate gland and bladder; 273 of these patients were in too uncertain a condition to warrant primary prostatectomy and so cystostomy was performed. Of the 4 patients who died from embolism, 2 had had cystostomy as a preliminary to prostatectomy; both patients were more than 70 years of age.

METHOD OF REDUCING THE INCIDENCE OF POSTOPERATIVE EMBOLISM

In order to combat the decrease of metabolism, the decrease in blood pressure, and the slowing of circulation, tablets of desiccated thyroid gland in doses of 2 grains, administered 3 times daily, have been used in all cases except those in which there has been an abnormal increase in pulse rate and temperature occurring as a spontaneous postoperative reaction. Cases in which the desiccated thyroid gland is not given will comprise approximately 10 per cent of the total number. Inasmuch as the increase in temperature and pulse rate in this small group occurs spontaneously, which means an increase in metabolism and flow of blood, it has not been felt necessary to add further to the reaction by the administration of desiccated thyroid gland. The administration of desiccated gland is begun as soon after operation as the gastro-intestinal tract tolerates fluids and drugs, usually from the second to the fourth days, and is continued until the

patient is out of bed, usually the tenth day. In any event the administration of the gland is stopped by the twelfth day. If marked elevation of pulse rate and temperature occur, it is discontinued sooner. In 3 cases compound solution of iodine (Lugol's solution) was given to counteract its effect, which it did successfully and without harm to the patient.

Since an increase in metabolism, which also may mean an increase in both temperature and pulse rate, is the primary object of giving the desiccated gland, it cannot be considered a deleterious effect. Other untoward effects have not been noted. If, during its administration, the patient is nauseated or vomits, it is discontinued. Also patients have been urged to move in bed, to flex their legs and arms, and especially to turn themselves from side to side, as advised by Wilson and Pool. Not infrequently even on a surgical service in which such a regimen is considered a routine procedure, one may find an occasional patient who, during the surgeon's absence, has not moved from the position in bed in which he was placed when he returned from the operating room or who has not received the desiccated thyroid gland. This emphasizes the necessity in each case of the surgeon seeing to it that whatever regimen is outlined should be carried out, for if this is relegated to others, its importance may not be recognized. Such a regimen has been used during the last 4½ years in the management of 4,500 surgical cases on my service, consisting for the most part of intra-abdominal operations on the gastrointestinal, the biliary, and the genito-urinary tracts.

The method of reducing the incidence of fatal postoperative embolism described might be expected to have a field of application in all cases except those of elderly patients with marked cardiovascular disease or disease of other parenchymatous organs which has weakened and debilitated the patient. On the surgical service of my colleague, C. F. Dixon, this regimen has been followed in all cases (except cases of hyperthyroidism) during the last 2 years, without a death from postoperative pulmonary embolism.

Undoubtedly there are factors other than slowing of the rate of metabolism, lowering of

blood pressure, and possible retardation of circulation that are responsible for the formation of thrombi and emboli, else the incidence of postoperative embolism would be much higher. It seems reasonable, however, that they set the stage, and whether infection, as may be inferred from Rosenow's isolation of streptococci from emboli at necropsy, or changes in blood or tissue fluids are the exciting factors is as yet undetermined. However, lowering of blood pressure, depression of metabolism, and possibly slowing of the circulation as a result of prolonged rest in bed, with great diminution of peristalsis and the restricted excursion of the diaphragm, following operation play an important part in either the predisposition to, or the causation of, postoperative thrombosis and embolism. Attempts have been made to overcome these changes through increasing the metabolic rate by the use of tablets of desiccated thyroid gland and early movement of the patient in bed.

SUMMARY

In a study of 267 cases of fatal pulmonary embolism following 63,347 major operations during the 10-year period from 1917 to 1927 at The Mayo Clinic, Henderson found the average incidence of fatal postoperative embolism to be 0.34 per cent.

The use of a regimen directed toward increasing the rate of metabolism, of blood pressure, and of blood flow in 4,500 major surgical procedures of comparable type during the last 4½ years has been followed by an incidence of fatal pulmonary embolism in less than 0.09 per cent of cases.

Of the 4 patients in this series who had pulmonary emboli, 3 were aged 70 years or more, and of those, 2 died from other causes (sepsis in 1 case and uræmia in the other). The age of the third patient was 54 years, and in this case auricular fibrillation was present. In each of the 4 cases there was myocarditis at necropsy; it was marked and associated with coronary sclerosis in 3 cases. These 4 cases illustrate the predisposition of patients with cardiovascular disease to the development of postoperative emboli, and emphasize the part played by disturbances of the blood flow in their formation.

Fatal pulmonary embolism did not occur among patients in good general condition when the described regimen of prevention was carried out.

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DISCUSSION

DR. EDWIN M. MILLER, Chicago: The endeavor of the essayist in this piece of clinical research is worthy of commendation, for though the incidence of fatal postoperative pulmonary embolism is relatively small, the fact that the accident usually happens with such frightful suddenness and with such surprising unexpectedness, often at a time

when the patient is well on the way to recovery, would make any well defined program directed toward its elimination, or even reduction in frequency, more than welcome. We have heard presented such a method, adequately tested, and of proved value. Nothing, it would seem on the face of it, should stand in the way of its acceptance.

General acceptance, however, of any new therapeutic measure, no matter how attractively presented, seldom is quickly gained, because first must be overcome a natural reluctance due partly to lack of knowledge of the new procedure and partly to faith in existing methods, a frame of mind which stimulates one to investigate all phases of the proposition before being convinced of its merit.

What are the facts surrounding cases in which a fatal pulmonary embolism has followed an operation? From a review of reports published within the past few years, especially from the German clinics, and from information received directly from pathologists, the following statements may be made without reservation:

1. The incidence of proved cases is very small.
2. The majority of the patients are well advanced in years, usually above the age of 60.
3. The operation is usually on the midportion of the body, especially the lower abdomen or pelvis.
4. The pathological condition is very frequently a carcinoma.
5. The accident is most apt to occur during the convalescent period, without pre-existing œdema, swelling of the legs, thrombophlebitis, or any other clinical sign which would attract the attention of the clinician to a likelihood of its occurrence.
6. At autopsy the site of origin of the thrombus is almost always found to be in the iliac or pelvic veins, or right auricular appendage. The length, caliber, and shape of the clot are sometimes the only clues to its origin, because of the almost constant absence of any local inflammatory change in the endothelial lining at the original site.
7. After giving due consideration to the influence of the multitude of factors which may or may not contribute to the etiology, the outstanding single factor concerned is stasis of the blood in the large veins of the pelvis.

What, then, may be done to influence this situation? Certainly much may be accomplished by methods already at our disposal: (a) careful preoperative study of each case, especially in those of advanced years, providing aid through digitalis to a weak or failing circulation; (b) careful operative technique—clean-cut dissections, accurate hæmostasis, and avoidance of mass ligation and undue pressure on great veins by retraction; and (c) diligent postoperative care, the paying of particular attention to adequate fluid intake, and intelligent use of digitalis, caffeine, or other drugs acting directly on the circulation. Tight bandages should be avoided, and especially should the free mobility of the chest be preserved. Frequent change in the position of the patient, the encouragement of early systematic exercise

of the arms and legs, and especially daily elevation of the foot of the bed as a mechanical method of increasing the venous flow from the dependent pelvic region, are important in the prevention of stasis of the blood.

It is a question in my mind whether, having done these things in the hope of avoiding a fatal pulmonary embolism, much more would be accomplished by the use of thyroid extract, unless it is definitely shown that, on account of the slight rise in metabolism which follows, the rate of flow is accelerated or the pressure elevated in the great veins of the pelvis, which are most commonly the original site of the thrombus.

DR. VERNON C. DAVID, Chicago: While an average of from 1 to 3 instances of postoperative pulmonary embolism usually occurs in large clinics in every 1,000 cases operated upon, there seems to have been a decided increase during the last few years. This may be more apparent than real, as Detering of Frangenheim's Clinic has pointed out, for in a chart covering the incidence of embolism since 1900 in the Cologne Clinic there was seen to be nearly as marked an increase in 1909 as there has been in the last few years. However, between the years 1923 and 1926 there has been a threefold increase in postoperative pulmonary embolism in Schmieden's Clinic and this is typical of many other clinics, including those of Rost and Bier. Concurrent with this has been the relative increase of thrombosis in patients after operation. Fatal embolism in non-operative cases and in medical cases also has increased during the same period but not as rapidly. In 30,000 cases in the Chemnitz Clinic, Martini reports an incidence of 0.22 per cent fatal postoperative embolism from 1917 to 1928 while 0.1 per cent occurred in patients who were not operated upon.

Clinical details. The usual time of appearance of postoperative embolism has been between the sixth and tenth days after operation. The majority of instances occurred in patients between 50 and 70 years of age. Obesity seems to be a predisposing factor. The type of anaesthesia seems to have no causative relation. In some statistics, cancer was present in as many as 33 per cent of the patients. Preceding infection, such as influenza or tuberculosis, is commonly present in the antecedent history.

The type of operation seems to play an important predisposing rôle in postoperative embolism. Abdominal and pelvic surgery leads the list in about 70 per cent of the cases. Stomach surgery, especially for cancer of the stomach, and pelvic surgery, particularly operations for prostatic hypertrophy and fibroids of the uterus, are the most important. Gall-bladder surgery and surgery of the large bowel, including removal of the appendix, also are followed by fatal embolism. Hernias, too, play rôles, while surgery of the extremities is rarely complicated by embolism. Thyroid surgery is particularly free from postoperative embolism. It is of interest in this

connection that Frund from the Garre Clinic has reported a decrease in the number of postoperative emboli following the administration of thyroid extract to patients about to be operated upon.

Tempsky tabulated a series of operations for carcinoma of the stomach, carcinoma of the rectum and appendicitis, from the Kuttner Clinic, in relation to postoperative thrombosis and embolism. In 1,458 cases of carcinoma of the stomach there were 49 postoperative thrombi and 12 emboli. In 496 of these cases, resection of the stomach was done with 17 postoperative thrombi and 5 emboli, which is at the rate of 1 embolism in every 100 cases.

In 506 cases of carcinoma of the rectum there were 27 postoperative thrombi and 17 emboli. Of these cases, 304 resections of the rectum were performed with 23 postoperative thrombi and 12 emboli or nearly 5 to every 100 cases.

Contrasting sharply with this was the report of 1,767 cases of appendicitis in which there were 20 thrombi and 4 emboli or 2 to a thousand, which is about the usual rate.

Pathological anatomical considerations. While visible peripheral thromboses of the internal saphenous vein are most common, fatal postoperative emboli rarely originate from this source, as it is found that 50 per cent of postoperative pulmonary emboli have their source in the femoral or iliac veins (Lubarsch). While occasional thrombosis of these veins may occur because of direct trauma, from a mass ligature, or from the direct action of an infectious process, in most instances these veins are not in the immediate operative field. The underlying cause of thrombosis must be discovered in factors not purely obvious.

Of these the importance of slowing of the circulation in veins has been emphasized by Ashoff and his school as an important factor predisposing to thrombosis. The platelets and white blood cells linger in the periphery of the vessel where the stream is the slowest and lay down on the endothelium of the vessel a white coagulum from which a thrombus starts. The factors influencing slowing of the blood stream in the large veins occur not infrequently in surgical patients. Among the most important of these factors are loss of blood, shock, loss of fluids from catharsis or excessive perspiration, weak heart action, and interference with the action of respiratory movements due to the pain of abdominal incisions. Of all the cases having postoperative embolism, Bauer from Koenig's clinic stated that about one fourth were noted to have cardiovascular lesions before operation but that at autopsy the heart was found to be affected in 95 per cent.

Ribbert has emphasized the importance of *injury to the intima of the blood vessels* in promoting thrombosis. Endothelium occurring in any of the structure of the body, including the veins, is subject to injury and degenerative changes by reason of infections, toxins from cancer growth, injury from the use of intravenous medication, and many other agents. Thrombosis is especially likely to occur where, in

addition to the injury of the intima of the veins, the blood stream is also slowed.

The third contributing factor, and possibly the most important, is the change taking place in the blood itself after operations, especially after operations on patients who are aged, who have cancer, who have cardiovascular disease, or who have recently undergone severe general infection. Bancroft and his collaborators have shown, after careful blood studies, that patients with postoperative thrombosis and embolism have an increase of blood clotting factors in their blood and usually a diminished amount of anti-thrombin. Govaerts, at the International Surgical Congress this past summer, advanced the interesting theory that injury to the blood platelets with their consequent viscosity brought about by infection was a primary cause of postoperative thrombosis. He said it was a common finding to recover micro-organisms from the clot causing the embolism.

Martin recently published the results of some interesting experimental work on postoperative embolism. He created emboli by the injection of iron chloride intravenously and watched under X-ray the thrombus proceed to the lung. Its course was slow and vacillating through the vena cava and occasionally it passed backward against the blood stream. When it reached the region of the diaphragm, it shot forward into the heart, aided by the sucking action of the accessory movements of respiration. From his study he believed that thrombi which did not occlude the vein or which reached beyond their point of vessel wall attachment into a larger vein were most apt to be detached and become emboli.

Prevention. Until more definite facts are known concerning the mechanics and chemistry of blood coagulation, our efforts must be aimed at removal of factors which predispose to thrombosis.

Before operation the patient should be out of bed as much as possible and fluid should be taken freely on the days preceding the operation. Purges *preceding the operation* with their consequent loss of body fluid should be avoided. If there is any question about the strength of the heart, digitalis should be given, but intravenous medication should be avoided. Varicosities of the extremities should be lightly banded with bias cut flannel bands.

At the operation, extreme care should be taken to avoid loss of blood and trauma, such as mass ligatures. Heavy mechanical retractors should be avoided.

Postoperative procedure. The patient should not be allowed to remain in one position during the first few days when so little inclination exists to move. The position of the legs should be frequently changed, and in almost all abdominal surgery the patient should be turned on the side for certain periods during the day. Tight abdominal dressings should be avoided. The fluid content of the bowel should be maintained. Heart stimulants should be used where cardiovascular incompetence is suspected. In accordance with the recommendation of Walter and Frund, small doses of thyroid extract may be given.

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