Some Reflections on Mortality Due to Anesthesia

E. M. Papper, M.D.

Rational assessment and accurate evaluation of the contribution of anesthesia to death in surgical patients are difficult problems. Implicit in the large collection of papers dealing with this subject is the fact that death from anesthesia should never occur. Furthermore, it is often suggested, if not definitely stated, that if death does occur in an anesthetized patient that there must have been some error of omission or commission.

Even classical literature carries this same implication. In Act IV of Romeo and Juliet, Scene 1, when the Friar talks to Juliet he describes the administration of a drug which presumably causes total anesthesia, simulates death and yet permits of a full and complete recovery. He says to her:

Take thou this vial, being then in bed, And this distilling liquor drink thou off; When presently through all thy veins shall run A cold and drowsy humour; for no pulse Shall keep his native progress, but succense; No warmth, no breath, shall testify thou livest; The roses in thy lips and cheeks shall fade To paly ashes, thy eyes' windows fall, Like Death, when he shuts up the day of life; Each part, depriv'd of supple government, Shall stiff and stark and cold, appear like death; And in this borrow'd likeness of shrunk death Thou shall continue two and forty hours, And then awake as from a pleasant sleep.

The purposes of this essay are to show the difficulties of accurate assessment of the anesthetic contribution to surgical mortality, to indicate the importance of reducing our ignorance of the causes of anesthetic death and to assume full responsibility for our acts even when we cannot document them completely.

Among many useful reports on this subject is the excellent paper of Dripps et al. which is a careful documentation and detailed dis-

cussion of the contribution of anesthesia to surgical mortality.¹ This kind of information and the massive collection of 600,000 anesthetics and the anesthetic deaths in these patients by Beecher and Todd document the available facts and point out the difficulties in precise understanding of some of the ways in which anesthesia can kill.²

Consideration must be directed (as all observers have indicated in their discussions) to the best possible comprehension of the actual role of anesthesia in causation of death in surgical patients.

Apropos of the problem of defining the role of risk in predicting mortality, Keats made an interesting comment on the usual methods of assessment of surgical risk by the physician, the surgeon and the anesthesiologist.³ He pointed out quite convincingly that any prediction of surgical mortality is subject to a high degree of error because of our failure to assess risk adequately. Presumably if risk is high and properly assessed, appropriate measures could be taken, at least in some instances, to reduce the mortality rate. Keats defined risk as a hazard or danger of exposure to loss or injury. In a manner similar to the prediction of insurance tables, risk can actually be determined when one examines past surgical experience and a probability figure for mortality can be ascertained for various surgical procedures. It is possible to outline what the probability of death from a given surgical or anesthetic procedure will be; but it is impossible to estimate the precise risk for a specific patient.

Keats then discussed those factors which predispose to an increased mortality from anesthesia and those which do not. For instance, risk for patients with cardiovascular disease was examined. It was concluded that well-treated patients who had congestive heart failure or healed myocardial infarction appeared to do very well during anesthesia and operation. On
the other hand, patients who have recent or repeated myocardial infarctions or the anginal syndrome; or patients with unrecognized coronary or myocardial disease who have unexpected complications at operation, are quite likely to have a higher mortality.3 Mortality is also higher in emergencies than in elective operations, in radical than in conservative operations, is related to the nature of the disease and the nature of the operation undertaken, and finally to the fact that in emergency operations underlying risks may be overlooked.

The estimate of the death rate from anesthesia has varied considerably in different reports. A common figure quoted is one in 1,500, which is very near the figure of the Beecher-Todd report.2 In some studies, the question of race is argued; there are studies indicating that mortality is higher in Negroes and others that it is not. The problem of age is considered also and is also a matter for disagreement. The question of the role of relaxants is also a subject of controversy.

Keats concluded his comment on retrospective studies with the observation that one learns little more than the fact that the sicker the patient the more likely he is to die, whether or not he is operated upon and whether or not he is anesthetized. The retrospective method of study was criticized mostly for its inability to predict what will occur with any given patient.3 This criticism may be an illusion. What will occur often has as much to do with the skill and judgment of anesthesiologist and surgeon as with the patient’s illness. In any overall study the matter of skill may not be apparent.

This discussion of the difficulties of understanding the risk of anesthesia and operation with specific reference to predicting the outcome of any given procedure on a given patient leads inevitably to a consideration of the validity of our estimations of anesthetic mortality. It seems, without question, that one could attribute a death that occurs in a patient to an anesthetic error if it occurs as the result of an act of ignorance or the improper application of an anesthetic agent or method to a clearly documented healthy patient. There is no doubt that such deaths occur from individual acts of ignorance or error in the light of available knowledge at the present time. However, these causes of anesthetic deaths are not only clearly preventable but, according to the study of Dripps and his colleagues, did not occur in a group of healthy patients, rated physical status I, with a large variety of anesthetic agents and methods.1 Unfortunately, preventable deaths due to anesthesia in healthy patients will occur unpredictably and inevitably because of human fallibility despite the enviable experience of the Pennsylvania study. One can maintain with reasonable certainty that not all anesthetics have been and will be given with this happy outcome in this country or in other parts of the world. However, it does indicate that such a situation is possible and it indicates further that any deviation from this happy state of affairs can be judged and diagnosed with accuracy beyond a reasonable doubt. In short, it seems quite clear that if a healthy patient dies during or consequent to a surgical procedure the reason for his death ought to be demonstrable by careful analysis of the clinical, toxicological and pathological features of the patient’s medical and anesthetic experiences. One could say, therefore, that these single, in contradistinction to collective, acts of ignorance can be diagnosed by the application of value judgments to an analysis of the course of events. One must emphasize, however, that complete honesty in appraisal of the anesthetic experience, the provision of accurate records of what transpired and the completion of autopsy and toxicological examinations must be carried out to insure a high degree of accuracy in estimating these causes of death.

In contrast, in patients who are sick, a death during or after operation is often difficult to analyze in any terms, including the role of anesthesia.

For example, one could consider a death due to “natural causes,” implying by this term a death that might have occurred at home, in a restaurant, in the theater or even in the hospital with no relationship whatever to the anesthetic and surgical experience. If a patient happened to die of one of many “natural causes” during the induction of anesthesia, it might be impossible to sort out the causal relationship. It is not sufficient to state that a death occurring during the induction of
anesthesia must be due to or associated with that anesthesia.

One must now consider the problems of accidental timing and the problems of collective ignorance in evaluating causes of death either due to anesthesia or to other causes. An interesting case problem illustrates this situation rather well. A patient aged 64, known to have moderately severe arteriosclerotic heart disease, but considered to be an acceptable surgical risk under the circumstances, was scheduled for gastric resection in the early evening. The situation was not an acute emergency but operation was deemed advisable without significant delay. The patient was known to have a duodenal ulcer and was admitted to the hospital with bleeding which was slow enough to be treated effectively with transfusion. The indication for gastrectomy was the failure of bleeding to stop after a reasonable period of observation and transfusion.

The patient was brought to the operating room in preparation for this orderly and well organized procedure. The anesthesiologist delayed his induction of anesthesia in order to confer with the surgeon about the details of transfusion management which were to follow. To accomplish this purpose and waste as little time as possible, the anesthesiologist left the patient in the induction room in the care of a junior colleague and went to the dressing room where the surgeon was changing his clothes. Both individuals walked back to the induction room together approximately five minutes later and found the junior anesthesiologist administering oxygen under intermittent positive pressure to the patient. He described a set of circumstances during which the patient became pale, made a small convulsive movement and ceased to breathe. Immediate palpation for peripheral pulses indicated that none could be felt and the blood pressure could not be measured. Since this unfortunate set of circumstances occurred in the days before closed chest cardiac resuscitation, a decision had to be taken whether to open the chest for cardiac massage. It was decided not to attempt this form of resuscitation because of the nature of his heart disease and the delay in time. One could quarrel with this decision in retrospect but it appeared wise at the time. Autopsy revealed a slowly bleeding duodenal ulcer and confirmed the presence of diffuse myocardial disease. Certainly neither of these events could be considered absolutely incompatible with life on the basis of structural disorders. One can speculate with interest on the role of anesthesia in causing death if the anesthesiologist had not decided to confer with the surgeon at that particular time and had in fact begun the induction of anesthesia. Since no important and unexpected findings at autopsy which could account for the sudden death were observed, many surgeons and anesthesiologists would have decided that this was a death due to anesthesia because no surgery was being performed, the patient had no lesions incompatible with life, and anesthesia induction had begun. It would not have been possible to provide accurate evaluation of the role anesthesia would have played had the induction begun. Such events may coincide to the point where a temporal association of an anesthetic event with death may lead to the erroneous conclusion that anesthesia had a causal relationship to death. It seems best in the state of our ignorance about some of these matters to consider that a death of this type should be classified as unknown in relation to anesthesia since the possibility exists that it might have occurred even in the absence of anesthesia if no clearly defined errors were committed. This point of view is in conflict with those who state that our progress is best served by leaning over far enough backwards to accept all potential causes of death as associated with anesthesia in order to work harder to understand why anesthetic agents may tip the balance unfavorably.

Another problem in trying to assess the possible causation of death is seen in the patient who, because of one disease, may actually die at any time and yet has a surgical lesion which, in the opinion of his medical and surgical advisors, will surely be fatal if uncorrected by surgical intervention. Hence a decision to operate is made in the full realization that there are two diseases potentially lethal; one at any time and one eventually. A clinical problem of this kind came to our attention in the form of a 72 year old woman who was known to have a carcinoma of the colon with
beginning obstructive signs and symptoms. She also had advanced arteriosclerotic heart disease, manifested by bouts of ventricular tachycardia, anginal pain and congestive failure. The major cardiovascular problem was the precipitation of ventricular tachycardias with relatively minor stimulation. Ventricular tachycardia was precipitated by such minor treatments as a barium enema, a proctoscopic examination, or a period of intense "nervousness." Attempts were made to modulate these episodes of ventricular tachycardia by digitalization and the use of quinidine. In the opinion of the physician, the frequency and severity of these episodes was favorably altered by drug treatment. With all these problems properly assessed and agreed to, induction of anesthesia was begun and the patient intubated with the aid of thiopental, oxygen and succinylcholine. Continuous electrocardiographic monitoring showed a rapidly developing ventricular tachycardia which led to ventricular fibrillation. Since this possibility had been anticipated, effective closed chest resuscitation, followed in due course by external electric defibrillation, was successful and no further arrhythmic episodes during ethylene-oxygen anesthesia occurred.

In assessing the role of anesthesia in what might have been a death, one comes into an area of difference of opinion. There are anesthesiologists who would maintain that the process of intubation with the method described would clearly predispose such a patient to ventricular tachycardia and fibrillation and should be considered an error in anesthetic judgment. On the other hand, others competent in assessing and managing patients ill with cardiovascular disease would find such an approach entirely acceptable. Finally, whether one agrees or not that this method of intubation is safe, one must be reminded of the fact that this patient, with no apparent cause or with minor provocation, developed these arrhythmias outside of the surgical operating room. Should one consider a death, if it occurs under these circumstances, as due to anesthesia or should one simply say that an anesthetic method or agent, like many other experiences in life to which these kinds of patients are subjected, was the final straw that ended a life in a manner which could be predicted with some certainty from previous clinical experience? One is not wise enough at this time to speak with any confidence on whether this kind of event should be considered related to anesthesia. It appears to be sufficient at present to indicate that in the value judgments of assessing mortality due to anesthesia one must be willing to accept the fact that an anesthetic event can be associated with death in a temporal sense without necessarily being causally related to it.

The viewpoint presented in this portion of the discussion emphasizes the need to recognize coincidence, unknown factors, and inevitability as the associated elements in the causation of anesthetic deaths. The danger in this attitude is that it may foster irresponsibility and denial of cause and effect relationships. It may even be a retrogressive force since it can provide an easy refuge to the irresponsible. The first step in this way of thinking can be to admit ignorance and the next to deny responsibility.

One could argue with pertinence that death is never "natural" and that as knowledge improves the areas of inevitability shrink. This attitude is best expressed by the converse of the traditional view; i.e., the physician is guilty until proven innocent. This concept holds that the anesthesiologist and the surgeon, together or separately, are responsible for a death if it occurs, even though the cause is completely unknown.

In short, it must be proven that death would definitely have occurred had there been no decision to operate. A patient who is moribund, in shock from severe injury will die if unoperated upon. It can never be shown with absolute certainty that a patient with heart disease would have died anyway.

This position has the great moral force that it always accepts responsibility for death even though the link is tenuous or invisible between cause and effect. It has the additional merit of stimulating clinical and basic research. It is deficient, however, in trying to sort out the elements that cause death—and tends to lump them in the term "operative death." Unless the anesthesiologist can and does share with the surgeon and physician every decision, including the decision to operate, it is difficult to see how he can rationally participate in a
responsibility function when he is often presented with a sick patient for the administration of anesthesia. Surely, in these circumstances, it does little to advance our thinking to say he is responsible for something he did not plan—and, in the event of death, where he applied all available knowledge to no avail.

It seems that these points of view can be reconciled to a considerable degree by recognizing that death is caused by something—even though it may be unknown in nature. The futility of saying that death must be the anesthesiologist’s responsibility if associated with anesthesia can be removed or at least minimized if he truly participates in the clinical judgments leading to operation. Then he can and must accept responsibility. This responsibility is not the question, “Is the patient safe for anesthesia?” The proper question in which he should have a voice is, “Assuming the illnesses of the patient, the surgical problem to be solved and the risk of anesthesia together—should anesthesia and operation be undertaken?” Progress in this direction is to be sought for the future. Then, and only then, can the anesthesiologist feel his obligation most fully.

These concepts can be extended to any phase of the preoperative, operative, and postoperative periods. For example, if the surgeon retracts the great veins and prevents adequate filling of the heart, this is obviously a surgical error and may cause death. However, the anesthesiologist can and should share this responsibility in a well ordered world of mutual respect. He should have detected a serious impact on the circulatory integrity of the patient, informed the surgeon to this effect and asked him to look for the cause of this difficulty in the surgical field. This kind of shared responsibility is really our goal—and it will reduce in number those deaths due to “coincidence,” “natural causes” or unknown factors.

One must consider the question further of the verification of the cause of death by objective methods in the hands of the pathologist. Except under very special circumstances, it appears to be agreed that the pathologist is often not able to help in answering the question of the relationship between an anesthetic experience and the cause of death. In an interesting description of this problem Angrist pointed out that physiological disruptions, among which anesthetics are involved, may not be reflected in structural tissue alteration and that the absence of a structural change does not in any way imply that anesthesia either was or was not causally related to death. In fact, the point is made in this discussion that the mechanisms which cause death are often multiple, complex and quite difficult to analyze. It is his opinion that a listing of a single cause of death may actually be impossible.

The difficulties and objections as to the validity of death certificates is discussed more fully by Treloar. It is not adequate, in short, to hope for a definitive solution of the diagnosis of death due to anesthesia from the pathologist in either his role as a toxicologist or a microscopic pathologist. The pathologist himself is only too keenly aware also of the inadequacies of the death certificate method of evaluating the relationships between clinical events and causes of death. Among these problems in the evaluation of deaths must be included the administration of anesthesia.

These deficiencies of pathological diagnosis appear to warrant renewed efforts on the part of the anesthesiologist to extend his ability to detect physiological and biochemical derangements during anesthesia and operation. Death due to a functional disorder of body function is as lethal as death accompanied by histological change. There can surely be no argument against the proposition that the more one knows about the patient the more effective can be the recognition of danger—and the diagnosis of the cause of death if necessary. Since one knows that sick patients die more often if anesthetized and operated upon than healthier patients, it is clear and unmistakable that precise collection of appropriate data, often called monitoring, is increasingly important.

Psychiatric factors may be involved in the relationship between the administration of anesthesia and subsequent death. There is an association in the minds of many surgeons and anesthesiologists between the “death wish” and the ultimate demise of the surgical patient. There has, in fact, grown up almost a body of mythology in which many responsible anesthesiologists and surgeons become deeply con-
cerned when a patient announces calmly and
with certainty that he is going to die during
or after an operation. Every experienced cli-
nician can remember one or more of such in-
stances in his practice and some become deeply
concerned about it. He often forgets the sur-
vivors, curiously enough. It has been obvious
an sober reflection that the acceptance of an
almost mystical relationship between death due
to anesthesia and the effect of a patient is
a self-defeating point of view to follow. Al-
though catastrophes can occur, the attitude
evolving from these considerations should be
to ask for psychiatric advice and guidance for
the patient prior to the administration of anes-
thesia and the performance of operation. This
kind of problem underlines the importance of
an adequate preanesthetic interview and as-
essment of the patient's mood as well as his
physical status. Several such patients who were
were treated properly medically and psychia-
trically were safely conducted through an anesthetic
and surgical experience. These psychiatric
factors, as possible contributory causes to anes-
thetic deaths, must be judged more precisely.
They can be important if unrecognized and
untreated in the preanesthetic period. It
seems from the evidence available at the
present time that such deaths need not occur
and the anesthesiologist and surgeon should be
able to give up the myth that some mystical,
supernatural force has dispatched a given pa-
tient to his ancestors and that this catastrophe
was beyond clinical control.

It has been documented in various ways
that the sicker a patient is the more likely
he is to die from anesthesia. The most clearcut
statement of this association is found in the
report of Dripps et al. The question then
naturally arises as to how to place a precise
evaluation on the degree of sickness.

Should one conclude that sick people are
more likely to die in any event and that anes-
thetics act as contributing factors to death?
Or can we deny that anesthesia has any bear-
ing on the cause of death in sick patients?
Under these circumstances it is safer and more
responsible to assume that something in the
anesthetic process might be causally related to
the death of a sick patient. There is, at the
present time, no precise knowledge which
bears upon this question and no way of know-

ing what the anesthetic process does to cellular
function to become either a contributory or a
primary cause in the disintegration of the
function of the cell which ultimately leads to
death. It would be very useful to have precise
studies of the effect of anesthetic agents and
anesthetic procedures upon the intimate met-
abolism of the vital organs. Such data are
known only in a fragmentary way. Further-
more, the available data have been collected
in animals or in healthy, normal human sub-
jects. Almost no knowledge is available on
the influence of anesthetics on abnormal organs
in patients who are sick enough to die should
further interfere with the function of the vital
organs take place. Clearly, such studies
would be of enormous value and it is to be
hoped that in the future, measurements of
alterations in the characteristic functions of
the heart, brain, liver and kidneys will take
place under conditions of anesthesia in pa-
tients with a variety of diseases. Studies of
the disorganization of enzyme systems, hor-
monal elaboration or the control of electrolyte
or water balance in patients with serious ill-
ness subjected to anesthesia are also needed.
Finally, although by no means completely, it
is evident that the influence of anesthetic drugs
on single cells and the more intimate structure
and function of these single cells, must be
obtained if our knowledge of these processes
is one day to be improved. Such studies fortu-
nately are beginning, but probably consider-
table time will elapse before adequate precise
knowledge of these influences will be felt in
the clinical anesthetic management of patients
with advanced disease.

Until the time arrives when these kinds of
data are available for clinical anesthetic
practice, one must accept the concept that
anesthetics do interfere in some manner as yet
unknown and contribute either directly or in-
directly to the dissolution of life and that
responsibility for these events must be ac-
cepted by the anesthetic community. The
entire matter must be considered as part of
our collective ignorance as distinguished from
the individual ignorance or error of knowledge
already available for application to patients.
The area of collective ignorance must be
diminished by precise study, intelligent clinical
observation, and a considerable amount of
intellectual receptivity to new ideas both scientific and clinical if one is to make adequate progress in this direction.

Summary

A consideration of the problems involved in assessing the relation of risk of anesthesia to mortality was discussed. Questions were raised about the validity of clinical judgments in actually assigning the cause of death to anesthesia in many circumstances where this is difficult and probably impossible to do.

A plea was entertained for the diagnosis of death due to anesthesia only where a clear and unmistakable error of commission or omission was effective in the light of well-established scientific and clinical knowledge.

It was also urged that those areas which are at best related only temporally to anesthesia should at the present time be considered as unknown insofar as their influence on death on anesthesia is concerned, but that responsibility of the anesthesiologist should not be abdicated or minimized.

Finally, it was suggested that an area of collective ignorance exists wherein no reasonable relation between the clinical events and death due to anesthesia can be established. Some suggestions were made as to how this area of collective ignorance may be diminished by appropriate scientific and clinical study.

References


HUMIDITY  The water loss from the human body during operation was 70–150 g./hour, of which only 3–12 g./hour was excreted through the lungs. Latent heat of vaporization of water from the lungs similarly represents only a small part of the total heat balance in the body. Prolonged use of closed-system anesthesia or humidification of respiratory gases during anesthesia does not significantly affect heat balance in the body, but other environmental conditions such as room temperature, room humidity and clothing exert a much greater influence on body temperature. (Sato, T.: Significance of Humidity in Anaesthesia (Japanese), Jap. J. Anaesth. 12: 131, 1963.)

KALLOCAINE  The LD₉₀ of kallocaine, 2-(dimethylaminoethoxy)-benzoic acid ethylester, in mice was 430 mg./kg. by subcutaneous administration, while that of lidocaine was 330 mg./kg. By the method of the intracutaneous wheal in guinea pigs, kallocaine was 4 times as effective as lidocaine and 4–8 times as procaine, and this effect was markedly augmented by adrenaline. In plexus anesthesia in the frog, the effect of kallocaine was nearly equal to that of lidocaine or procaine. No irritant action of kallocaine was observed on the skin and mucous membranes in rabbits. The depressor action of kallocaine by intravenous injection was weaker than that of procaine and stronger than that of lidocaine. (Fujita, Y., Takagi, H., and Yamada, H.: Pharmacological Studies on Kallocaine, a New Local Anaesthetic (Japanese), Jap. J. Pharm. Chem. 35: 1, 1963.)