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Controlling the Airway

Skill and Science

IN 1874, Jacob Heiberg wrote that during chloroform anesthesia, noisy, obstructed breathing, particularly during inspiration, could be prevented by pulling the jaw forward. He was not sure how this worked and proposed freezing a corpse to find out.[1] Unfortunately, I have not been able to find any report of this proposed study, which was conceived without the advantage of modern imaging methods. Even earlier, writers had suggested that obstruction of the airway in unconscious subjects often could be overcome by pulling the tongue forward, and they suggested that the "inelastic ligaments" between the tongue and epiglottis would act on the epiglottis, which was considered to be the cause of the problem. If this method failed, then intubation of the trachea was advocated,[2] which could explain why we are perhaps more skilled in using instruments to keep the airway patent than we are informed about how the body does it. Indeed, tracheal intubation has been with us for a millennium.[2] It is only now, with modern methods of investigation and imaging, that we are unraveling the complexities of how the airway is controlled. Thus, in an early study, Boidin[3] used a fiberscope to show how head position affected the epiglottis, and Nandi *et al.*[4] showed how the epiglottis moved with head extension. This issue of ANESTHESIOLOGY contains two studies of the airway during anesthesia.[5,6] Such investigations are important for several reasons, despite the increasing variety of apparatuses being marketed to hold the upper airway open. First, all of the devices that we could choose have disadvantages, from minor morbidity caused by an apparatus in the airway,[7] to the dangers associated with misplacement and blockage, to the apparent risk of transmission of serious disease,[8] of which, in Europe, variant Creutzfeldt–Jakob disease is the latest worry. Simple, safe methods of airway management with minimal intrusion could have many advantages. Second, after anesthesia, the control of the airway has to be relinquished to the patient, and in many other circumstances, patients' control systems may be impaired, either by disease or deliberately during sedation. In some cases, the consequences of poor airway control are striking and disastrous, but in others, the consequences of inadequate airway control are not clear. In patients with overt, sleep-disordered breathing, a study conducted over 4 yr showed a "dose" relationship with hypertension.[9] Perhaps airway obstruction is a cardiovascular stress that plays a part in complications such as postoperative myocardial ischemia and infarction.

Anesthesiologists are ideally positioned to study and understand these phenomena. We spend our career maintaining the airway, often with our own hands. We attempt to predict, maybe optimistically,[10] when we may encounter difficulties with the airway; we address the consequences of returning control of the airway to the patient after anesthesia;[11] and we are aware that sedation may lead to adverse events.[12]

An early study of the upper airway muscles concluded, "The simultaneous contraction of opposing muscles maintains airway patency."[13] The reality is more complex: the activity of the pharyngeal muscles is not simple, and there are clear differences between the different muscles. In conscious subjects, muscle activation is affected by factors such as breathing route, posture, and blood pressure. The control of pharyngeal muscle activity has both central and reflex components.[14] Anesthesia of the airway reduces airway muscle activity in patients with sleep-disordered breathing and can induce airway obstruction during sleep in normal subjects.[15] General anesthetics reduce the central component of this control.[16] The coordination of the respiratory muscles is complex, particularly the interaction of some of the less accessible muscles of the velopharynx,[17] but the muscles in this region are vital in the interaction between the jaw, the pharynx, and airway resistance.[18,19]

Studies of anesthetic actions in this field have been few. In the past, the pharynx has been a "border post" between specialties, and studies of the respiratory system were usually conducted after the upper airway had been bypassed and "secured." When obstructive sleep apnea became recognized as an important cause of morbidity, research on airway control impairment in this condition accelerated, and we gained knowledge of how the normal airway is controlled. However, there are important differences between the normal airway and the airway in sleep apnea and associated conditions such as obesity. One striking difference is in the shape of the pharyngeal airway, which is narrowed from the side in obesity.[20] In obese subjects, the circumference of the

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neck is an independent predictor of sleep apnea.[21] Although we know that sedative and anesthetic agents disturb airway control,[22,23] and there can be clear differences between different types of sedatives,[24] the precise effects of depressant drugs have not been investigated. Since partial neuromuscular block has little effect on airway patency,[25] and local anesthesia of the airway can cause obstruction,[15] I suspect that the afferent and central parts of the system are those mainly affected. The Starling resistor model of airway collapse predicts that resistance upstream of the point of collapse is important, since that resistance regulates the pressure at the point of airway collapse. There may be simple clinical steps we can take to reduce the likelihood of collapse by optimizing this part of the airway.

Airway obstruction in sleep apnea syndrome can also cause transient lung abnormalities and perhaps may worsen gas exchange.[26] Episodic hypoxemia in patients after surgery has been linked to airway obstruction and is considered by some to be analogous to sleep apnea syndrome. Breathing problems after surgery are certainly common in patients who already have impaired airway control.[27] Although episodic postoperative hypoxemia has been associated with morbidity, such as cardiac ischemia[28] and delirium,[29] these are merely observational links, and it is not clear if hypoxemia, in general, impairs outcome from surgery. Oxygen therapy is widely used to prevent hypoxemia, but it does not affect the number or severity of the episodes of obstruction. Nasal continuous positive airway pressure can overcome airway obstruction in sedation and anesthesia,[30] but this treatment is ineffective after surgery.[31]

In the studies in this issue of ANESTHESIOLOGY, airway muscle activity was either very small or deliberately abolished.[6] Consequently, these studies tell us about the physical properties of the passive upper airway, which is affected by internal pressure, flow, and gravity when it is not affected by important muscle activity. Eastwood *et al.*[5] showed that when the depth of anesthesia was reduced, the pharynx became less collapsible. Similar findings have been reported in sedation with midazolam.[32] It is not yet clear how much small or residual quantities of anesthetic and sedative agents disturb the control of the airway. This topic is difficult to study because of the sleep state of the patient. When aroused, airway control may be satisfactory, but when left alone, the same patient may have persistent airway obstruction or may show repeated cycles of obstruction and recovery.[33] I find that a useful feature of impending airway difficulty is the "poof" sign that comes from expiration through a lax mouth, indicating diversion from the nasopharyngeal route, which is normal in conscious subjects.

What can we learn from these studies? Perhaps we should measure neck circumference rather than thyromental distance! We should certainly consider nasal obstruction as a potential cause of airway difficulty. We should think more about the efficacy of the maneuvers we apply,[19,34] not just in terms of the measures used in the present studies, but in terms of how we can judge how well the airway is maintained (a magnetic resonance imaging scan is not often at hand) and in terms of important clinical outcomes that could be related to how well we can maintain the airway.

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Hemodilution and Candles

THE impetus for the development of transfusion-sparing pharmaceuticals or techniques has been the risks associated with transfusion (infectious disease, transfusion-associated lung injury, transfusion reactions [hemolytic, anaphylactic], immunomodulation) and the need for augmenting oxygen delivery when compatible blood is not available or cannot be used. The blood supply of North America and Western Europe is now safer than ever; however, the need for blood and blood components at times is greater than their availability.[1]

Acute normovolemic hemodilution (ANH), withdrawal of blood while maintaining isovolemia, was originally introduced to return coagulation factors to the patient after cardiopulmonary bypass.[2] The concept that hemodilution might save erythrocytes *per se* appears to have been first envisioned by Messmer *et al*.[3] The basis of this notion is that ANH reduces the circulating concentration of erythrocytes, thus, following ANH, the blood lost during surgery contains a lesser concentration of erythrocytes than if ANH had not been performed, resulting in a conservation of erythrocytes. ANH is one of the few procedures in medicine that lends itself to mathematical modeling. Analyses have shown that efficacy of hemodilution requires high initial hematocrits,[4,5] low hematocrits after ANH ("target"),[4,5] and a surgical blood loss that exceeds a specific minimum value[4,5] and is also within a specific range.[5] Recently, a more detailed analysis concluded that for ANH to be efficacious (conserve at least one unit of erythrocytes), surgical blood loss should be more than approximately 70% of the patient's blood volume.[6]

Although the use of ANH to conserve erythrocytes and transfusion has been advocated by several organizations[7–9] and transfusion experts,[10,11] its use has remained controversial because of its uncertain efficacy and safety. The authors of a recent meta-analysis noted that their findings were inconclusive.[12] The expected inconclusive nature of the totality of all publications rests on several important issues. Studies have failed to fulfill one or more of these critical criteria, all of which are required to provide a valid test of hemodilution: a relatively homogeneous population of patients so that blood loss is reasonably uniform; prospective random allocation of patients to groups with or without ANH; sufficiently high initial hematocrit; sufficiently low hematocrit ("target") after ANH; withdrawal of a sufficient volume of blood; prospective transfusion criteria, uniformly and consistently applied; surgical blood loss that is within the range of potential efficacy; and a sample size sufficiently large to have a reasonable expectation of detecting a difference, should one exist. Indeed, of the publications analyzed, it appears that none satisfied these criteria.

In this issue of ANESTHESIOLOGY, Matot *et al.*[13] report the results of their study, which was uniquely designed to meet all criteria to provide an adequate test of the efficacy of ANH. They removed approximately 2 l of blood during ANH, reducing the patients' hematocrit from 41% to 24%, and found the technique to be efficacious, significantly decreasing the fraction of patients requiring allogeneic transfusion (from 36% to 10%). Their findings are in accord with the prediction that more than 70% of a patient's blood volume must be lost for ANH to be efficacious,[6] and that there is a range of blood loss, above and below which ANH will not result in avoidance of allogeneic transfusion.[5,6] Also, as predicted by mathematical analysis,[6] in the study conducted by Matot *et al.*[13], when blood loss was within the range of potential efficacy (70–90% of the estimated blood volume), ANH

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was exceedingly efficacious: none of the nine patients in whom ANH was performed required allogeneic blood, whereas all 10 patients in the control group did ($P < 0.0001$); and the groups had an equal incidence (100%) of allogeneic transfusion when blood loss exceeded 90% of the patient's estimated blood volume (numbers of patients not transfused supplied by personal communication with I. Matot, June 21, 2002). When surgical blood loss is exceedingly high, ANH can reduce the number of allogeneic units of blood transfused but not the fraction of patients requiring allogeneic transfusion.[5,6] It is important to note that the efficacy of ANH depends not only on the amount of surgical blood loss but also on a sufficiently high initial hematocrit and the removal of a sufficient quantity of blood to achieve a sufficiently low "target" hematocrit.[4–6]

The removal of such substantial quantities of blood and the reduction of the hemoglobin concentration to values sufficient to produce efficacy has the potential to threaten patient safety. Normovolemia must be maintained (to preserve oxygen delivery to and oxygenation of critical organs) not only during but also after performing ANH of a substantial fraction of the patient's blood, as the administered fluids leave the vascular space at different rates.[14,15] Although the reduction of the hemoglobin concentration to a value as low as 5 g/dl does not produce systemic evidence of inadequate oxygenation in healthy, conscious humans,[16] it does produce subtle, reversible deficits of cognitive function.[17,18] Anesthetized patients can withstand hemodilution to hemoglobin concentrations at least as low as 8 g/dl (and likely substantially lower) without systemic evidence of inadequate oxygenation.[19,20] It has been recommended that anesthetized healthy patients not be transfused until the hemoglobin concentration decreases to 7 g/dl[21] or 6 g/dl.[8] The safe limits of hemodilution for patients who cannot increase blood flow sufficiently to critical organs (*e.g.*, because of arterial stenosis, vasculitis, or impaired cardiac function) are not known. Hemodilution has not been associated with systemic or cardiac markers of inadequate oxygenation in patients undergoing coronary artery surgery.[22,23] The coronary vasculature has a reserve dilatory capacity, which, in response to acute anemia, can increase blood flow by several fold.[24] However, data from laboratory studies clearly demonstrate that at very low hemoglobin concentrations (below 3–5 g/dl), the myocardium becomes hypoxic,[25] with decreased contractility,[26] and that the hemoglobin value at which this occurs is higher when coronary artery blood flow is limited by a stenosis.[27]

As other studies before it, the present study did not evaluate a sufficient number of patients to document the safety of ANH. For example, it would not have been expected to be able to detect an increase in myocardial infarction rate in this group of American Society of Anesthesiologists physical status I and II patients. Even in patients with or at high risk for coronary artery disease undergoing abdominal aortic surgery, the incidence of myocardial infarction is only approximately 4%. A study with an 80% likelihood of detecting a 25% increase of this incidence, to 5%, would require approximately 14,000 patients. Detection of a doubling of this rate, to 8%, would require a study population of approximately 1,200 patients.

Thanks to Matot *et al.*[13], we now have appropriate evidence that ANH, as predicted, can be efficacious if used correctly for the appropriate patient population. Unfortunately, its safety is unknown and must be weighed against the risks of the procedure and those of allogeneic transfusion. In addition to the potential risks of not maintaining normovolemia (hypovolemia or hypervolemia), theoretically, ANH could cause an increase in surgical blood loss because of increased blood flow (owing to increased cardiac output[16,28,29] and lower blood viscosity[30]); decreased concentrations of clotting factors[31] (they are removed together with the erythrocytes); the effect of the fluid, such as hetastarch (on coagulation factors and platelet function[32]), infused to replace the withdrawn blood; and perhaps because of altered margination or function of platelets.[33,34] Although some investigators have reported increased surgical blood loss with ANH, Matot *et al.*[13] did not. In addition, ANH requires expertise, takes time, and potentially could also divert the attention of the anesthesiologist from other patient care issues.

The potential for blood components to transmit viral disease is at an all-time low in Western Europe and North America, with the risk for transmission of human immunodeficiency virus (HIV), hepatitis C virus, and hepatitis B virus each being estimated as approximately 1 per 1,900,000, 1 per 1,600,000, and 1 per 180,000 units transfused, respectively.[35,36] The risk of fatal hemolytic transfusion reactions (the majority occur in the operating room) exceeds that of transmission of HIV or hepatitis B virus.[37] However, the incidence of transfusion-induced serious bacterial infection is at least as high as that of either HIV or hepatitis C virus, and it has been suggested that the incidence may be substantially underestimated.[38] In some areas of the world, the incidence of transmission of parasitic disease is substantially higher than that of viral disease.[39] New vectors of transmissible disease may, and likely will, appear. In addition to the infectious risk, the consequences of potential immunomodulation[40] and the incidence of transfusion-associated lung injury[41] are not clearly defined.

Thus, we are left with a not unusual clinical circumstance. We can quantify the efficacy of a technique or therapy, but its full risks are not clear. Is it worth the candle?[42] It is better to light a single candle than to curse the darkness (attributed to Confucius): with the efficacy having been shown, perhaps someone will now address safety.

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Preparing for Bioterrorism

"AMERICANS," wrote Thomas Jefferson, "love peace, yet spurn a tame submission to wrong." In the wake of September 11th and October 4th, our adversaries have learned this lesson well.

Yet our decisive military victories and response to the anthrax attacks have been tempered by the knowledge that bioterrorism remains a genuine threat. Unlike traditional warfare, the battle against devastating bio-organisms cannot be won on a battlefield. It must be achieved in the laboratory, the emergency room, and the local clinic and hospital.

The anthrax mailings of last fall forced us to reevaluate our ability to respond effectively to acts of bioterrorism. We have done that, and we have acted.

The President's budget for 2003 calls for $518 million to enhance preparedness at the nation's hospitals to respond to incidents of biological or chemical terrorism. This funding represents a 284% increase over the amount provided this year.

The President's budget supports a variety of activities to prevent, identify, and respond to bioterrorism. These include: epidemic detection and response; maintaining and securing the National Pharmaceutical Stockpile; performing research to improve our methods, training, and health care service delivery; and assisting our state, local, and other federal partners in improving our capability to respond to an emergency. This funding will also provide resources to expand the capacity of hospitals and outpatient facilities to confront large scale casualty incidents; improve capabilities to control infection and treat individuals at risk for a communicable disease; training in recognition of rare diseases and treatment of toxic exposures; and such infrastructure improvements as infectious disease containment systems.

The budget includes another $100 million for bioterrorism training for health care professionals, poison control centers, and emergency medical services for children.

We also have provided $1.1 billion to states and several major cities to help them build public health infrastructures capable of responding quickly to sudden disease outbreaks. States and localities submitted plans that we approved in a matter of months—in some cases, weeks—and we have released the funds to help equip first-responders with the resources they need.

This is the first time that federal, state, and local governments have come together on a unified plan to strengthen our public health system and better prepare to respond to a terrorist attack. The importance of this fact cannot be overstated. For the first time, we're working together and are on the same page. Now that we have plans, we need to get on with building. The grant money will allow that to take place. In addition, state and local public health workers and hospitals must have access to adequate supplies of medicines, and must be trained to receive and distribute these essential supplies once they are delivered. So, we have purchased enough antibiotics to treat 20 million people exposed to anthrax, and enough smallpox vaccine for every American. With the recent donation of smallpox vaccine by Aventis Pasteur (Lyon, France), we can respond in an emergency even sooner than we had anticipated.

Public and private-sector initiatives alike are needed, since our nation's physicians and nurses stand in the first line of defense against potential incidents that could involve large-scale casualties. They must be ready to respond effectively. With careful planning, adequate funding and sound execution, they are becoming better prepared than ever to meet the challenges of a bioterrorist attack.

Yet even their tremendous work will be insufficient if we lack an adequate food inspection system and thereby leave ourselves open to bioterrorism through our food supply. We are committed to hiring 655 new field staff for food safety. Hiring and training these new inspectors is FDA's top priority, and I am pleased to report to you that FDA has nearly all of these men and women, just 5 months after these funds were provided. As these inspectors are trained, FDA will double physical examinations of food imports in FY 2002, and double them again in FY 2003. We have also asked for an additional $17 million just for food safety above the 2003 request.

While food safety has been FDA's most visible role in protecting against bioterrorism, I have also asked for an additional $5 million for blood safety efforts. FDA must expand its capacity to ensure the availability of safe blood and blood products at the time of an emergency.

The Department of Health and Human Services has worked hard to provide timely, accurate, and readily understandable information about dealing with bioterrorism to health care professionals. For example, the Centers for Disease Control and Prevention publishes breaking reports on bioterror and public health-related news in its 'Morbidity Mortality Weekly Reports.'

This Editorial View accompanies the following article: Abraham RB, Rudick V, Weinbroum AA: Practical guidelines for acute care of victims of bioterrorism: Conventional injuries and concomitant nerve agent intoxication. ANESTHESIOLOGY 2002; 97:989–1004.

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David C. Warltier, M.D., Ph.D., served as Editor-in-chief for this Editorial View.

The CDC also produces fact sheets, guidelines, news briefs, announcements, and video and satellite broadcasts about bioterrorism on its Web site. The site has received more than 6 million visits and 14 million requests for information since September 11th. . In addition, the Agency for Healthcare Research and Quality (AHRQ), an agency within HHS, initiated a new Web site to teach hospital-based physicians and nurses how to diagnose and treat rare infections and exposures to bioterrorist agents such as anthrax and smallpox.

The site was designed by researchers in the Center for Disaster Preparedness at the University of Alabama at Birmingham under a contract from AHRQ. It is the first of its kind to offer free continuing education credits in bioterrorism preparedness to clinicians. The site offers online courses for emergency department clinicians, including physicians, nurses, radiologists, pathologists, and infection control practitioners. You can check it out at http://www.bioterrorism.uab.edu.

In the article by Drs. Abraham, Rudick, and Weinbroum[1], you will read sound medical counsel concerning how to help patients suffering from both conventional injuries and bioterrorism—and how to do so on a large scale. I urge you to study this article carefully and consider how you, as a medical professional, can best ready yourself and your staff for critical care, anesthesia, and other medical needs of significant numbers of people affected by biological or chemical agents in combination with trauma.

Thanks to each of you for your commitment to your patients and to our country. We at the Department of Health and Human Services are proud to be your partners in this effort.

Tommy G. Thompson, B.S., J.D. Secretary of Health and Human Services, U.S. Department of Health and Human Services, Washington, D.C.

Reference

1. Abraham RB, Rudick V, Weinbroum AA: Guidelines for acute care of victims of bioterrorism: Conventional injuries and concomitant nerve agent intoxication. ANESTHESIOLOGY 2002; 97:989–1004