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## KEY POINTS

- Led by the discipline of anesthesiology, simulators and the use of simulation have become integral parts of many health care domains for various uses including training of novices, advanced residents, and experienced professionals; research about and with simulation; system probing; and performance assessment. Patient simulation can be part of an organization's patient safety strategy and supports building a culture of safety (see [Chapter 6](#)).
- A wide variety of simulators are now available. The pace of technical development and applications is fast. Nevertheless, technology alone does not teach. The use of simulators needs to be consistent with the target population and the learning objectives. Different simulators may be best suited for different purposes; for some scenarios and teaching goals a standardized patient (actor) may be more effective.
- The most widely used simulators in health care are computer screen-based simulators (micro-simulators), and part-task trainers mocking parts of a human body or mannequin-based simulators most often used for resuscitation training and complex team training. Complex simulation team training with mannequin-based simulators are often referred to as "high-fidelity" or "full scale" patient simulation training.
- The development of mobile and less expensive simulator models allowed for substantial expansion of simulation training to areas and locales where this training could not previously be afforded or conducted (so-called *in situ* simulation training).
- When used for education and training, the simulator device alone does not teach. It is merely a tool to accomplish learning objectives that are difficult to achieve during real patient care. The design of programs, curricula, scenarios, and debriefings, as well as the ability of simulation instructors to create appropriate learning opportunities are the crucial factors that determine whether the simulation tool is effective in achieving the relevant goals.
- The greatest obstacles to providing effective and relevant (high-fidelity) patient simulation training are (1) obtaining access to the learner population for the requisite time, and (2) providing appropriately trained and skilled simulation instructors to prepare, conduct, debrief, and evaluate the simulation sessions.
- The most important component of high-fidelity patient simulation training is the self-reflective (often video-assisted) debriefing session after the clinical scenario. The quality of debriefing strongly depends on the training, skills, and experience of the instructors. Thus, special training for developing patient simulation instructors is needed that goes beyond the instructor qualifications for ordinary clinical teaching. Most methods of debriefing emphasize open-ended questions and inquiry to trigger self-reflection and insightful analysis, leading to deep learning by the learner group.
- Simulation scenarios need clear learning objectives for both clinical and nonclinical skills (human factors, see [Chapter 6](#)). Scenarios need to take into account the target population, learning goals, relevance, and in-scenario guidance. Maximum realism is not always needed. For high-fidelity patient simulation team training, the *anesthesia crisis resource management* course model (ACRM, often referred to as CRM, developed by one of the authors [David Gaba], see [Chapter 6](#)) is a popular approach worldwide for human factor-based simulation training in anesthesiology and health care. The 15 CRM key points help individuals and teams to be aware of human factor-related pitfalls, apply different safety strategies, and enhance human performance and patient safety.
- In terms of research, simulation has proven valuable to study relevant simulation aspects such as debriefing methods, scenario design and conduct, and program development. It also was found to be valuable to study human performance during anesthesia, including human factors and failure modes in care.
- In regard to system probing, simulation can be used successfully for the testing of an organization's structures and processes, such as the early detection of system failure modes and the preparedness for major events, the development of new treatment concepts (e.g., checklist design and use, telemedicine), and the support of bioengineering system development (e.g., device beta-testing, educating the manufacturers' workforce).
- With a view to assessment and evaluation of performance, a variety of assessment tools and behavioral markers have evolved that offer a new window on performance. Nevertheless, when simulation is used to assess and evaluate human performance, the unique constraints of simulation (which is never like the real thing) need to be taken into consideration.

## What This Chapter Is About: An Overview

*“Simulation training in all its forms will be a vital part of building a safer health care system” [p. 55].<sup>1</sup>*

SIR LIAM DONALDSON, CMO ANNUAL REPORT (2008)

In concert with other modalities, simulation can improve patient safety by informing personnel about best practices, guiding established clinical practice, and strengthening human performance. Unfortunately, simulation in health care is still not used as widely and systematically as needed, compared to its use in other high-risk/high-reliability industries. From the authors’ point of view, anesthesia professionals, anesthesia departments, and health care organizations need to strive to embrace the use of simulation for the many purposes mentioned in this chapter. Simulation, in combination with human factors training (CRM, see [Chapter 6](#)), has the potential to substantially improve the quality and safety of health care.

Anesthesiology has pioneered the field of simulation in health care. The rather new, mannequin-based patient simulators have been in regular use in anesthesiology since the early 1990s. Over the last two decades, there have been many technologic advances in simulation and a wide variety of applications of simulation in anesthesiology have been developed in the domains of education and training, research, system and equipment probing, and assessment. Considerable collective experience has already been achieved with simulation devices, sites, pedagogy, and assessment rubrics. What was once an arcane and small niche activity has expanded enormously. Simulation can be thought of like playing a musical instrument: almost everybody can somehow coax a tone out of it, but to play it well and use it optimally can only come about after considerable practice.

This chapter aims to provide the reader—whether a simulation participant or a novice or experienced instructor—with a solid and nuanced understanding of many aspects of patient simulation in anesthesiology and other parts of health care.

Modern simulation with advanced teaching concepts and the integration of human factors training (CRM) is much more than traditional basic life support and advanced cardiovascular life support (“megacode”) training. Modern simulation team training is academically demanding, personally stimulating, and involves many disciplines and lines of thinking. As a simulation instructor, you are operating at the core of our profession!

### READERS WILL LEARN

- ... about the varying uses of simulation in anesthesiology and health care, mainly focusing on the topics of training and education, research, system equipment probing, and assessment and evaluation.
- ... to distinguish and classify different types of patient simulators (e.g., part-task trainers, simulators for low- and high-fidelity simulation, patient actors/standardized patients, hybrid simulation) and to understand their strengths and weaknesses.
- ... about the possibilities and limitations of different simulation-based training approaches regarding (1) simulation

site (e.g., dedicated simulation center, “in situ” simulation, mobile simulation); (2) simulation time (e.g., scheduled events vs. events on-call); (3) simulation participants (e.g., single discipline, multidiscipline, interprofessional).

- ... about educational and psychological factors that enable or inhibit learning in patient simulation, such as scenario design and conduct, the elements or phases of a simulation training, and debriefing techniques.
- ... about different multifaceted tasks of a simulation instructor and the need to acquire special skills to teach more complex and nuanced single-discipline or interprofessional activities.
- ... about the ecological validity of simulation and what is known about its benefits, costs, and cost-effectiveness.
- ... about the use of simulation for assessment of clinician performance and some of the issues and limitations thereof.

To cover those aspects, the authors have tried to balance retaining classic references, where the intellectual content has only changed slightly over the years, with newer ones that reflect either changes in thinking or evidence, or newer reviews and syntheses of knowledge and experience. Since simulation has become a key tool in addressing issues of patient safety and human factors in anesthesiology there is some degree of complementarity between this chapter and [Chapter 6](#).

In this chapter, the authors use “anesthesia professional” to refer to any anesthesia clinician taking care of a patient, whether a physician, certified registered nurse anesthetist (CRNA), or anesthesia assistant (or to similar positions in other countries).

### WHAT THIS CHAPTER IS NOT ABOUT

This chapter mainly addresses simulation in anesthesiology and presents the overall picture as seen by anesthesia professionals, intensivists, or others. Simulation devices and activities outside of the scope of perioperative management, that are strictly about psychomotor aspects of invasive procedures or surgery, and part-task screen-based simulators (e.g., Gasman) are at most only touched on briefly.

The chapter describes simulation in anesthesiology generically and does not address separately simulation for specific subspecialties. There is a sizable body of international experience with simulation in pediatric settings now that may be of further interest to some readers.<sup>2-9</sup>

Organizational aspects of simulation training and the topic of organizational implementation and sustainability of simulation programs are covered in [Chapter 6](#), where simulation programs are covered from an organization’s view among other organizational improvements to enhance patient and system safety. For more information on this topic, the reader is referred to the back part of [Chapter 6](#) (Box 6.13 in [Chapter 6](#) gives an overview).

## Simulation in Anesthesia: Why Is It Important?

**See one—do one—teach one?** Read one—do one—teach one? Many decades ago anesthesiology trainees might have been “given a long leash” (inadequately supervised)

and asked to gain experience by “sink or swim,” often with a clinical population of indigent patients. Using actual patients in this way as if they are expendable “simulators” is unethical, and the presumed learning experiences were extremely uneven. In the last few decades unacceptable practices have been eliminated, but it increasingly begs the question of how can clinicians at all levels of experience feel the difficulties of patient care, including managing very difficult situations, without putting patients at undue risk? How does someone go from a total novice to a fully competent independent anesthesia professional? And of increasing importance, how can clinicians—during both initial and recurrent training—learn and hone skills of dynamic decision making, situation awareness, leadership, communication, and teamwork?

Anesthesiology is a “hands-on” discipline. It is not likely for medical students and residents to learn simply by “looking,” “time passing,” or by “osmosis.” The application of (rare) technical skills, the correct use of medical knowledge and algorithms, as well as the reliable utilization of anesthesia nontechnical skills (see [Chapter 6](#))—such as teamwork, communication, and leadership behavior—need to be learned and then trained repeatedly. At the same time, experience is no substitute for excellence (see [Chapter 6](#)). This is especially true for nonroutine events, such as emergencies or rare complications. Not only trainees but also experienced clinicians require continuous education and training of their clinical and nontechnical skills in order to stay current and avoid bad habits or the normalization of deviance (see [Chapter 6](#)).

Health care, with anesthesiology as the pioneering discipline, borrowed and adapted alternative educational approaches to teach knowledge and gain procedural experience from years of successful service in other industries that faced similar problems. These approaches focused on “simulation.” Simulation is a technique well known in the military, aviation, space flight, and nuclear power industries. Simulation refers to the artificial replication of sufficient elements of a real-world domain to achieve a stated goal. The goals include for example education and training of technical and nontechnical skills, system probing, testing of equipment and supplies, and assessment as well as evaluation of students and personnel. These different topics are covered in this chapter, even though there is a focus on simulation as a training and education tool.

In 2000, the National Academy of Medicine (then the Institute of Medicine) released a report, *“To Err Is Human: Building a Safer Health System,”* that suggested the use of simulation training in health care in order to reduce preventable errors.<sup>10</sup> The American College of Critical Care Medicine recommended the use of simulation to improve training in critical care.<sup>11</sup> With anesthesiologists being the pioneers for simulation-based training in health care, simulation in anesthesia already has a long tradition. At the same time, its comprehensive and profound implementation has come a long and rocky way over the last decades and, despite many benefits, still needs further implementation and continuous evaluation. Major recognition of simulation in anesthesia by the clinical world is highlighted by the fact that it is now a highly utilized training course for the practice improvement component of Maintenance of Certification in Anesthesiology (MOCA) in the United

States.<sup>12</sup> In Australia and New Zealand, it is an integral part of anesthetic training.<sup>13,14</sup> In their reviews, Lorello and colleagues,<sup>15</sup> LeBlanc and colleagues,<sup>16</sup> and Higham and Baxendale<sup>17</sup> give an overview of simulation-based training in anesthesia. In many parts of the world, including industrial countries, the use of simulation is way behind the United States or Australia.

A fundamental part of the future vision for simulation is that clinical personnel, teams, and systems will undergo periodic and systematic simulation activities across their entire career using various modalities of simulation and for diverse purposes of education, training, performance assessment, refinement in practice, and system probing. This vision is inspired in part by the systems in place in various high-reliability industries, especially commercial aviation and nuclear power (see [Chapter 6](#)). Needless to say, using simulation as part of the process of revolutionizing health care is more complex than merely attempting to stick simulation training on top of the current system. Moreover, beyond training, simulation may provide indirect ways to improve safety, including facilitating recruitment and retention of skilled personnel, acting as a lever for culture change, and improving quality and risk management activities.

## Application of Simulation in Anesthesia and Health Care

Simulation techniques can be applied across nearly all health care domains.<sup>18</sup> A few books are devoted solely to the topic of simulation and its use in and outside of anesthesiology.<sup>19-24</sup>

In the upcoming section, an overview of the main objectives of simulation in health care and anesthesiology are presented in the following sequence: (1) education and training of technical and nontechnical skills, (2) system probing, (3) testing of equipment and supplies, (4) assessment/evaluation, (5) research, and (6) further purposes.

### USE OF PATIENT SIMULATION FOR TRAINING AND EDUCATION

With respect to the first objective—education and training—anesthesiology remains a driving force in the use of simulation in health care,<sup>25</sup> although simulation has spread to nearly every discipline and domain. As used in this chapter, *education* emphasizes conceptual knowledge, basic skills, and an introduction to nontechnical skills and work practices. *Training* emphasizes preparing individuals to perform actual tasks and work of the job.

Disciplines successfully applying simulation for training besides anesthesia<sup>15,26</sup> are, for example, emergency medicine and emergency field responders,<sup>27-29</sup> trauma care,<sup>30,31</sup> neonatology<sup>32-34</sup> and pediatric anaesthesia,<sup>2,3,5,35</sup> labor and delivery,<sup>36-38</sup> surgery,<sup>39,40</sup> radiation oncology,<sup>41</sup> intensive care,<sup>42,43</sup> and infectious disease.<sup>44,45</sup> Simulation serves almost all resuscitation trainings, which have advanced over the years.<sup>46</sup> [Fig. 7.1](#) gives several impressions of simulation training.

Nearly every anesthesia residency program in the United States offers some cogent simulation training experiences,



**Fig. 7.1 Different impressions of simulation training sessions in different health care environments.** Photos from left to right: (1) In situ simulation training on a ward. (2) In situ simulation team training in the anesthesia environment. (3) Simulation exercise during the annual simulation congress INSIM, Frankfurt Main, Germany. The photo shows a simulated patient that is rescued out of a crashed car. (4) Full-scale in situ simulation team training in the emergency department. (5) Military simulation training with Tactical Combat Casualty Training and Care under Fire conditions, *InPASS*. *Photo with permission by M. Rall.* (6) Simulation Training at the Simulation Center TüPASS in Tübingen, Germany. Shown is a handover moment where a traumatized patient is handed over from the ambulance team to the trauma team. *Photo with permission by director M. Rall 2010.* (7) Simulation training on the intermediate care unit. (8) Simulation exercise with a standardized patient that is rescued out of a crashed car. *Photo provided by M. Rall.* (9) In situ simulation training in an operating room (OR) showing the beginning of a full team obstetric scenario for emergency cesarean. The photo is taken through an OR window from the temporarily established simulation control room outside the OR. *(Photo provided by M. Rall.)*

although the scope, frequency, and target content vary. Other disciplines and other countries may not have adequate simulation training coverage during residency, as evidenced by a study by Hayes and colleagues.<sup>47</sup>

The military and the U.S. Department of Homeland Security also have been heavy users of simulation in health care; simulation has been applied to the initial training of new field medics and to the recurrent training of experienced clinicians and clinical teams.<sup>48</sup> In 2013, a first instructor course for the North Atlantic Treaty Organization (NATO) Special Operations Forces (SOF) was held at NATO headquarters in Brussels to bring together medical experts from the United States SOF, the NATO SOF, and some civilian instructor experts (including authors Rall and later Oberfrank).

Simulation is relevant from the earliest level of vocational or professional education (students) and during apprenticeship training (interns and residents), and it is increasingly used for experienced personnel undergoing periodic refresher training. Simulation can be applied regularly to practicing clinicians (as individuals, teams, or organizations; the latter for example for disaster drills, or for preparing to care for patients with Ebola virus disease<sup>49</sup>) regardless of their seniority, thus providing an integrated accumulation of experiences that should have long-term synergism. Thus, it is applicable to health care providers with a range of experience, including experts,<sup>50</sup> novices, advanced residents,<sup>25</sup> medical, nursing, other health care students,<sup>51-57</sup> and even children.<sup>58-61</sup> Simulation *rehearsals* are now being explored as adjuncts to actual clinical practice; for example, surgeons or an entire operative team can rehearse an unusually complex operation in advance by using a simulation of the specific patient.<sup>62,63</sup>

Many simulation centers offer continuing medical education (CME) and training for experienced practitioners, and many aspects of simulation training for residents can be expanded for this purpose. Several studies have shown that experienced anesthesiologists have deficiencies in the management of critical patient situations and make severe errors comparable to those of anesthesia residents.<sup>64-71</sup> Because crisis situations are rare during routine clinical work, these results are not startling. In addition, experience in terms of years on the job and hierarchy probably do not correspond to expertise and excellence. Crisis management training with patient simulation should be started early in education and training and applied on a recurring basis during practice.

Concerning education of health care professionals about patient safety, patient simulation can be a tool that contributes to changing the culture in an organization bottom-up to create a culture of safety. First, it allows hands-on training of junior and senior clinicians in practices that enact the desired culture of safety based on the principle of high reliability organizations (see *Chapter 6*).<sup>72</sup> Simulation can be a rallying point about culture change and patient safety that can bring together experienced clinicians from various disciplines and domains (who may be captured because the simulations are clinically challenging and show the need of change in direct relation to patient treatment), along with health care administrators, executives, managers,<sup>73,74</sup> risk managers,<sup>75</sup> and experts on human factors, organizational behavior, or institutional change. For these groups,

simulation can convey the complexities of clinical work, and it can be used to exercise and probe the organizational practices of clinical institutions at multiple levels (see section on system probing). Various curricula and recommendations for curricula development for simulation training exist.<sup>76-81</sup>

## USE OF PATIENT SIMULATION FOR SYSTEM PROBING AND PROTOCOL TESTING

In regard to the second objective, simulations that are conducted in actual patient treatment locations (referred to as “*in situ*” simulation, ISS) are powerful tools for testing (system probing) and evaluation of organizational practices (protocol testing).<sup>75</sup>

In a study comparing ISS to center-based simulations, ISS was related to more insights about processes in the organization and challenges with equipment.<sup>82</sup> Another study used simulation as a supplement to a Failure Modes and Effects Analysis (FMEA, see *Chapter 6*). In order to enhance system safety, FMEA is a risk management tool that proactively tries to enhance organizational learning by experts describing and identifying possible errors and their effects. Whereas adding simulation to that process did not result in more failure modes described, the process resulted in a richer description of how they would actually unfold in practice.<sup>83</sup>

Another way to probe the system is to identify active and latent failures during ISS of the treatment of patients. In Reason's famous error trajectory model to describe incident causation (known as the Swiss cheese model, see *Chapter 6*), incidents are seen as a combination of active (simplified: human) and latent (simplified: system) failures that interact to cause bad outcomes. Based on this model, a study<sup>84</sup> of 46 sessions of ISS training for handling emergencies was conducted with over 800 participants, with the goal to recognize and remedy active and latent failures in order to suggest where to invest resources. Of the total of 965 breaches, nearly 50% were classified as latent conditions, and the rest was classified as active failures. In another study, simulation was used to discover latent safety threats with the help of unannounced *in situ* simulation of critical patients in a pediatric emergency department.<sup>85</sup> Similarly, the “hemorrhage project” at Stanford assessed and trained the treatment protocol of life-threatening hemorrhage during several system-probing events using unannounced, simulation-based mock events, and successfully identified areas of improvement after probing.<sup>75</sup>

In 2016 simulation was used to demonstrate gaps in an organization's response system that could expose staff to Ebola once the emergency disaster response had been activated.<sup>86</sup> The simulation center had 12 hours to prepare simulations to evaluate hospital preparedness should a patient screen positive for Ebola exposure. Further simulation cycles were used during the next weeks to identify additional gaps and to evaluate possible solutions.

Furthermore, iterative simulation-based testing and redesign was shown to be of assistance when developing cognitive aids or protocols for all kind of crises, and to eliminate design failure. For instance, McIntosh and colleagues<sup>87</sup> used this approach to develop and test a new cognitive aid for the management of severe local anesthetic toxicity. Utilization

of formative usability testing and simulation-based user-centered design resulted in a visually very different cognitive aid, reinforcing the importance of designing aids in the context in which they are to be used.

Simulation has a role in designing new hospitals and departments—whether in terms of the physical layouts or in terms of work processes. Simulation can help in evaluating design ideas. Simulation can be used to facilitate moving into a new location, for example moving with staff and patients into a new intensive care unit (ICU) or a new hospital.<sup>88</sup>

Simulation is increasingly appreciated as a tool for risk management. Driver, Lighthall, and Gaba<sup>75</sup> argue that from a risk management standpoint, simulation has a number of potential ways in which it might prevent claims or mitigate losses. They called simulation “*a data source about clinical performance*” [p. 356]. De Maria<sup>25</sup> and associates demonstrated that a simulation-based approach can identify system-wide practitioner gaps in anesthesiologists and create meaningful improvement plans.

## USE OF PATIENT SIMULATION FOR TESTING EQUIPMENT AND SUPPLIES

With respect to the third objective—testing of equipment and supplies—patient simulation is being used in collaboration with biomedical industries. For example, some simulation centers offer training to executives, engineers, and sales representatives of equipment manufacturers. The simulator allows them to gain some understanding of the clinician’s task demands during patient care situations (including those of unusual stress) in which their company’s devices are useful.

Simulation has been used for research on human factor issues in the development of new monitoring and therapeutic devices. The simulator provides a unique test bed and demonstration modality for pre-procurement evaluation of the usability of medical devices from different manufacturers. In two of our affiliated hospitals (VA Palo Alto [DG] and Tübingen, Germany [MR]), simulation enabled us to conduct evaluations of prototype monitoring systems that were not yet approved for clinical use and could not be evaluated in a pre-procurement clinical trial.

Other industrial uses include training personnel in the use of novel pharmaceuticals. Simulators have been featured in a multifaceted approach to launch the opioid remifentanil in the United States and have been used to teach clinicians in the safe use of drugs, such as for example desflurane. Besides offering important educational benefits, industrial activities are an important source of income for simulation centers to help defray the costs of training students and residents.

## USE OF PATIENT SIMULATION FOR PERFORMANCE ASSESSMENT

With respect to the fourth objective, simulations have taken a central role in the evaluation and assessment of the performance and competence of health care students, residents, practicing physicians, and teams—for low-stakes or formative testing (education and training), to a lesser degree to-date for summative testing (certification, recertification, etc.), and for research on clinician decision-making

or on care processes. Assessment of performance for both clinical and nonclinical skills can be made in a variety of health care settings.<sup>64,69,89-98</sup>

Anesthesiology has taken a leading role in the development of simulation-based assessment.<sup>99</sup> In a review study in 2012, Boulet and Murray<sup>99</sup> summarized simulation-based assessment for education specifically in anesthesia. In a more recent systematic review in 2016, Ryall and colleagues<sup>100</sup> summarize the use of simulation as an assessment tool of technical skills across health professional education. They concluded that simulation is an effective assessment tool, but pointed out that the effectiveness as a stand-alone assessment tool requires further research.

Assessment with simulation held and still holds several challenges for research and education. Those include: (1) to determine aspects of performance to be measured, (2) to create reliable and valid scores and measurement tools, and (3) to find measures for both clinical and nonclinical performance. Furthermore, simulation itself poses several unique challenges and pitfalls that need to be taken into account, as discussed later in this chapter. Several assessment measures and scoring systems exist.<sup>99-102</sup>

Organizationally, in the United States, the Accreditation Council for Graduate Medical Education made the use of simulation a required component for anesthesiology residency programs. Recognizing its benefits not only for education and teaching of novices and residents, but also for the continuous education of certified practicing anesthesiologists, more recently simulation-based training in managing challenging situations leading to practice improvement was adopted as a favored component of the American Board of Anesthesiology’s (ABA’s) MOCA program. Whereas simulation as a tool for the formative assessment of performance during training of students and residents is already widely used in anesthesiology, it has still penetrated only modestly for the formative assessment (and less so for summative assessment) of practicing anesthesiologists,<sup>103</sup> raising new questions as described in a study by Weinger and colleagues.<sup>64</sup>

Because performance assessment is closely related to human performance, many results of simulation studies with this focus were already discussed in [Chapter 6](#), and the reader is referred there as well.

## USE OF PATIENT SIMULATION FOR RESEARCH

In regard to the fifth objective—research—simulation-based research falls into two categories: (a) research *about* simulation—testing or improving the techniques, technologies, and didactics of simulation; and (b) research *that uses* simulation as a tool to study other things, such as human performance and clinical cognition (see [Chapter 6](#)), or clinical care processes.<sup>104</sup> [Box 7.1](#) provides a sampling of these types of questions.

Regarding research *about* simulation, some examples would include the design of debriefing approaches such as Debriefing with Good Judgement,<sup>105-107</sup> Debriefing-Diamond,<sup>108</sup> PEARLS,<sup>109</sup> TeamGAINS,<sup>110</sup> and others<sup>111-114</sup>; methods for designing simulation scenarios such as PARTS<sup>115</sup>; the efficacy of using videos in debriefings<sup>116-120</sup>; the creation and maintenance of an inviting learning atmosphere<sup>121</sup>; the effective design of specific training interventions such as for resuscitation,<sup>46,122,123</sup> airway

## BOX 7.1 Exemplary Research Issues That Can Be Addressed by Using Simulation

### Cognitive Science of Dynamic Decision Making (see Chapter 6)

- What is the interaction of precompiled procedural knowledge (Type I thinking) versus deep medical knowledge and abstract reasoning (Type II thinking)?
- How does supervisory control of observation relate to vigilance, data overload, and visual scanning patterns?
- What is the information content and utility of watching the surgical field?
- How are optimal action planning and scheduling implemented?
- How does reevaluation fail and result in fixation errors?

### Human-Machine Interactions

- What is the distraction penalty for false alarms?
- Do integrated monitors and displays have an advantage over multiple stand-alone devices and displays?
- How easy to use are the controls and displays of existing anesthesia equipment in standard case situations and in crisis situations?

### Teaching Anesthesia in the Operating Room (see Chapter 6)

- How much teaching can be accomplished in the operating room without sacrificing the anesthesia crew's vigilance?
- How well can faculty members detect and categorize the performance of anesthesia trainees?
- What teaching styles are best integrated with case management in the operating room?

### Issues of Non-Technical Skills/Teamwork on Anesthesiologist Performance

- How does an anesthesia crew interact during case and crisis management?
- How is workload distributed among individuals?
- How do crew members communicate with each other, and how do they communicate with other members of the operating room team?

### Effects of Performance-Shaping Factors on Anesthesiologist Performance

- How do sleep deprivation, fatigue, aging, or the carryover effects of over-the-counter medications, coffee, or alcohol affect the performance of anesthesiologists?
- Can smart alarm systems or artificial intelligence provide correct and clinically meaningful decision support in the operating room or intensive care unit?

### Development of New Devices and Applications: Research Regarding Techniques of Simulation

- How well can simulations re-create perioperative clinical settings? Can they provoke the same actions as used in real clinical care (ecologic validity of simulators)?
- How much does debriefing add to learning from simulation? Are specific techniques of debriefing, or combinations thereof, of greater applicability or utility, overall or for particular situations?
- How do various aspects of simulation scenarios influence aspects of perceived reality, and how do they influence transfer of training into the real world?
- Does simulation training lead to better clinical practice and improved clinical outcomes?



**Fig. 7.2 Realistic patient simulation as a test bed for studying the performance of medical rescue teams in full chemical protection gear.** Teams wore normal uniforms or full protection suits while performing basic resuscitation actions (e.g., placement of intravenous lines, drawing up drugs, intubation). With full protective gear, communication within the team and with the patient (while still conscious) is difficult. (Photograph taken by M. Rall at the Center for Patient Safety and Simulation, Tübingen, Germany.)

management,<sup>124,125</sup> and avoidance of catheter-related infections<sup>126</sup>; and testing of specific training interventions such as for facilitating speaking up,<sup>50,127-129</sup> briefings,<sup>130</sup> and feedback.<sup>131</sup>

Patient simulation is now used sometimes to address the medical management of chemical, biologic, or nuclear threats from accidents, weapons of mass destruction, or terrorism. One group in Germany, used simulation to test the constraints of treating patients in full chemical protection gear to optimize the strategies of the German Ministry of Internal Affairs for dealing with terror attacks or chemical plant disasters (Fig. 7.2). Several investigators have performed multidisciplinary studies with combined simulation modalities (script-based simulators, model-based mannequin simulators, and simulated acted patients) to teach the management of victims of an attack with weapons of mass destruction and terrorism.<sup>132,133</sup> The demand for such training is substantial in nations engaged in active military conflicts or with an ongoing need to prepare for war or terrorist attacks.

Regarding (b) simulation as a research tool, it offers some unique features, and it can be thought of as a complementary window on the clinical world relative to other modalities. It can be applied, for example, when complex phenomena such as medical team processes are studied. Examples are investigations of how teams adapt from routine to non-routine situations and how this adaptation is related to performance,<sup>134-140</sup> communication processes such as information processing,<sup>141</sup> talking to the room<sup>142</sup> and speaking up,<sup>50,129,143-146</sup> problem-solving and decision-making,<sup>142,147-149</sup> and coordination requirements during resuscitation.<sup>139,140,150-154</sup> Important milestones for simulation-based research of both types was the creation by the Society for Simulation in Healthcare (SSH) in 2007 of its flagship peer-reviewed journal, *Simulation in Healthcare* followed in later years by other peer-reviewed journals (e.g., *Advances in Simulation*, *BMJ Simulation & Technology Enhanced Learning*, *Clinical Simulation in Nursing*). In addition, for research that is linked tightly to a specific clinical domain, the traditional medical specialty journals have become more welcoming to articles about simulation or that use simulation as an experimental technique.

Cooperation between simulation directors or instructors and psychologists, human factors engineers, or educators has proved useful in research and training. Such collaborations have helped delineate the theoretical foundations of simulation-based experiential learning, improve the understanding of debriefing, and research on work psychology and human performance in health care.<sup>155-161</sup> Many institutions have integrated psychologists or educators, or both, into their simulation center staff.

## OTHER USES OF PATIENT SIMULATION

Traditionally, simulation-based training is focused on health care professionals as the recipients. In recent years, simulation was opened up for new types of recipients. These studies are not conducted within anesthesia, but demonstrate innovative ways of thinking about simulation that might be adaptable in some form to anesthesia-oriented simulations. A study showed that the use of “standardized clinicians” to train patients to be more competent in their discharge conversations was feasible.<sup>162</sup> Patients interacted with role players in the role of the discharging clinician, practicing what to say and ask, as well as how to manage the medication they were supposed to take. The group around Kneebone involves patients in the design of simulations, opening simulation activities to them.<sup>163</sup> They use simulation in a demonstration mode that intends, for example, to give citizens an improved insight into what it is like to be in the hospital<sup>164,165</sup> or what care in the clinical context should feel like.<sup>166</sup> The aim is to diversify access to simulation beyond health care professionals.

Other unique applications of simulation have surfaced. Some centers use simulators for conducting outreach programs with high school or college students interested in health care. Patient simulators have been used to help produce educational videos on various patient safety issues. Simulation has sometimes been used to familiarize legislators or regulators with the realities and complexities of dynamic patient care.

Simulation has been used as adjuncts in medicolegal proceedings.<sup>167</sup> While current patient simulators cannot predict the exact physiologic behavior of a specific patient, simulations can be used to illustrate typical perioperative situations and the role of different monitors and therapeutic actions and to provide context for the patient management questions of the litigation.

The use of simulation training for strategic or operational coordination and decision making in health care logistics has been described.<sup>168</sup>

## History, Development, and Types of Simulators and Simulation

The following section gives a short, non-exhaustive overview about the history and the development of the main simulators in health care and anesthesia. For a more in-depth examination of the topic, the reader is referred to further literature. Particularly the mannequin-based simulators that are in wide use have been well covered in several review articles<sup>169-171</sup> and a whole book chapter by Rosen written in 2013 is dedicated to the topic in detail.<sup>172</sup> Another comprehensive textbook on the history of simulation in health care tracing it back 1500 years was published by Owen.<sup>173</sup>

**Simulation probably is as old as mankind.** Simulation has probably been a part of human activity since prehistoric times. Rehearsal for hunting activities and warfare was most likely an occasion for simulating the behavior of prey or enemy warriors. In medieval times soldiers learned the art of swordsmanship on dummy soldiers. Hundreds of years ago, models were used to help teach anatomy and physiology, and simulators were used to train surgical procedures and to help midwives and obstetricians handle complications of childbirth. Italy was the major source of simulators early in the 18th century, but in the 19th century, dominance in clinical simulation moved to France, Britain, and then Germany.<sup>174</sup> In modern times, preparation for warfare has been an equally powerful spur to the development of simulation technologies, especially for aviation, navy and armored vehicles. These technologies have been adopted by their civilian counterparts, but they have attained their most extensive use in commercial aviation. The aircraft simulator achieved its modern form in the late 1960s, but it has been continuously refined.

**Mannequin-based simulators (MBSS).** In 1969, the first electromechanical mannequin-based simulator in modern health care—Sim One—was produced by an aerospace company working with an educator and an anesthesiologist at the University of Southern California.<sup>175</sup> It consisted of a mannequin comprising an intubatable airway and upper torso and arms, and in many respects was years ahead of its time. It was originally used as an aid for students or residents learning to intubate, as well as to induce anesthesia but the project died out in the early 1970s. In the following years, several other mannequin-based patient simulators were developed and introduced in the middle to late 1980s. Noteworthy among others is Harvey, a cardiology mannequin

simulator released in 1976, which is able to simulate the arterial pulse, blood pressure, jugular venous wave, precordial movements, and heart sounds in normal and diseased states.<sup>176</sup> In 1986, a team at Stanford, headed at first by Gaba and DeAnda,<sup>177</sup> developed a full-scale simulator called the Comprehensive Anesthesia Simulation Environment (CASE); they used it initially to study the decision-making processes of anesthesia professionals during critical events,<sup>68,178,179</sup> but they were also interested in its use for training. Over a few years, with their recognition of the parallels with Crew/Crisis/Cockpit Resource Management (CRM) in aviation this team developed their flagship simulation training course Anesthesia Crisis Resource Management (ACRM, see [Chapter 6](#)).<sup>180,181</sup> Newer commercially-available mannequin-based patient simulators have been in use in anesthesiology since about 1995, and considerable collective experience with the devices already has been achieved. Currently, full-size mannequin-based simulation devices are used in most simulation centers (available now, for example, from the manufacturers Laerdal, Gaumard, CAE Healthcare, and others). Such devices allow the simulation of rapidly changing physiology and can support a variety of hands-on interventions (e.g., airway management, vascular cannulation, drug administration, electric countershock, or pacing). Some devices allow the system automatically to recognize injection of specific medications or therapeutic maneuvers, such as cardiac massage, and then—with or without instructor input—to respond in an appropriate manner.<sup>182</sup> Even though highly developed, mannequins still miss important features. [Box 7.2](#) shows desirable features of future MBS systems.

#### PATIENT SIMULATION ACTION BOX

From a patient safety and teaching point of view, it is a mistake to focus too much on complicated and nice-to-have features that the latest device might offer. Those features and add-ons will not necessarily improve simulations or benefit participants. High-fidelity simulation may be useful, but that will not necessarily require a simulation device with complex features. It is critical pedagogically, and economically, to match the simulation device to the target population and objectives of the simulation activity.

**(Computer) Screen-based simulators (microsimulators).** Beginning in the mid-1980s, several screen-based, also called screen-only simulators (microsimulators), were developed by anesthesiologists. These included (1) screen-based part-task trainers that simulated isolated aspects of anesthesia, such as the uptake and distribution of anesthetic gases in the body given different physiologic and physical chemistry situations (e.g., the well-known Gasman program<sup>183</sup>); and (2) screen-based overall-task trainers that represented nearly all aspects of the patient and clinical environment. Originally, the patient was represented by drawings or animations, but increasingly in these systems the representation of the patient is by photographs or videos. Vital signs

#### BOX 7.2 Desirable Features of Future Mannequin-Based Simulator Systems

- Ability to interface to or to mimic advanced brain monitoring such as: *AEP*, Auditory evoked potential; *BIS*, bispectral index; *EEG*, electroencephalographic; *PSI*, patient state index.
- Advanced skin signs such as: change in skin color to cyanotic or pale, improved diaphoresis, change in skin temperature (e.g., as a result of shock or fever), rash, hives, or generalized edema
- Regurgitation, vomiting, airway bleeding or secretions
- Physical coughing (currently only sounds are simulated)
- Realistic convulsions
- Purposeful movements of extremities
- Improved or possible support for spinal, epidural, or other regional anesthesia procedures
- Improved EEG signals (e.g., for BIS, AEP, PSI)
- Improved intracranial pressure
- Support for physical central venous and arterial cannulation
- Improved fetal and maternal cardiotocogram

*Please note: This list contains features that are not currently incorporated. Some features may be under development and could be available after publication of this book. In addition, some features are currently available as third-party or homemade add-ons.*

appearing on virtual monitors may mimic real clinical devices. Actions are selected typically using a graphic user interface, pointing and clicking on menus and buttons, and using sliders and numeric entry boxes to allow control of most kinds of interventions that clinicians use on a regular basis.

#### Part-task trainers and virtual procedural simulators.

In the 21st century, advancements in engineering and computer science have stimulated a new era of simulator technology, including:

- Part-task trainers in the form of anatomic mock-up devices that are made from synthetic material to represent human body parts, such as models that allow training of central line placement, epidural catheter insertion, cricothyroidotomy, or chest drainage. Over several decades, tissue-based simulation—representing some sort of part-task trainer—has become more common, with trainees no longer learning procedural skills using animal models because of cost and issues of animal rights.
- Virtual simulators for surgical and procedural skills (i.e., hardware and software that provide haptic feedback for performing realistic laparoscopic cholecystectomy, bronchoscopy, colonoscopy, echocardiography, and endovascular procedures).<sup>182</sup> In these systems, the synthetic (virtual) environment exists solely in the computer. The real procedure is performed by using a video display that can be recreated by the simulator. The person simulating the procedure interacts with the video display through the eyes (without or with head-mounted glasses) and the ears, and usually the hands, if the simulator features special instruments, instrumented gloves, or sensors. For anesthesia, for example, there exist VR simulators to train the conduct of fiber-optic intubation<sup>184,185</sup> and regional anesthesia.<sup>186,187</sup> Two systematic reviews are available for more in-depth information on the general use of simulation teaching regional anesthesia.<sup>188,189</sup>

**Virtual reality and augmented reality (usually via head-mounted displays).** Both immersive *virtual reality* (VR), which fully integrates the human user into the computer's world, and *augmented reality* (AR), which adds computer-generated imagery onto or next to the real-world view, typically use head-mounted displays to either replace ordinary vision or to augment it. Both approaches have been described in the literature, often in prototype or research-only settings. This chapter will discuss only VR and not AR. The authors (DG in particular) have been evaluating commercially available systems for head-mounted display VR. For health care they seem to fall into two categories: (1) *visualization* of objects or spaces—typically for anatomical structures, or for architectural environments, and (2) *physically interactive clinical environments*—meaning the clinicians themselves can move with the space and interact directly with each other and the virtually presented patient, essentially the VR equivalent of physical mannequin-based simulation. Visualization applications are much more common and are direct applications of consumer VR hardware and software (e.g., visualizing the human heart in all its detail inside and out instead of, say, the Taj Mahal). Fully interactive VR makes use of commercial head-mounted displays and other gear but is more complex to create the clinical space, patient, and equipment while providing for multiple physical participants to interact with seamless head and body movements.

Both types of VR are still in quite early stages of practical implementation in health care and how these approaches can best be used in health care remains to be seen, but the tide is now turning away from arcane research or “vaporware” to an era of rapidly improving practical devices and applications. Although Gaba has previously written that VR would soon (by 2020-2025) completely replace all physical simulation, this now seems unlikely in that time frame; in fact, it is likely that VR will join the spectrum of simulation modalities each of which has a set of unique advantages and disadvantages relative to the others.

**Virtual Environment/Virtual World.** A related type of virtual simulation is the *virtual environment* or *virtual world*. According to Wikipedia, a virtual world is a computer-based simulated environment intended for its users to inhabit and interact through avatars (users' graphic representation of themselves). Such systems typically allow multiple participants to control their own avatars (including speech) simultaneously over a network and to interact verbally and by virtual physical actions within a commonly perceived virtual environment. This technology currently portrays the virtual world as perspective three-dimensional images (or possibly true 3D) on a computer screen with sound. Virtual worlds are most commonly used for computer games. In a medical virtual world, the patient may be an automated avatar controlled by the computer, or the patient may be an avatar inhabited by a human participant. Kleinert and colleagues published a review of such systems in 2015 and concluded that the development and validation of such simulators will need to be the subject of further research.<sup>190</sup>

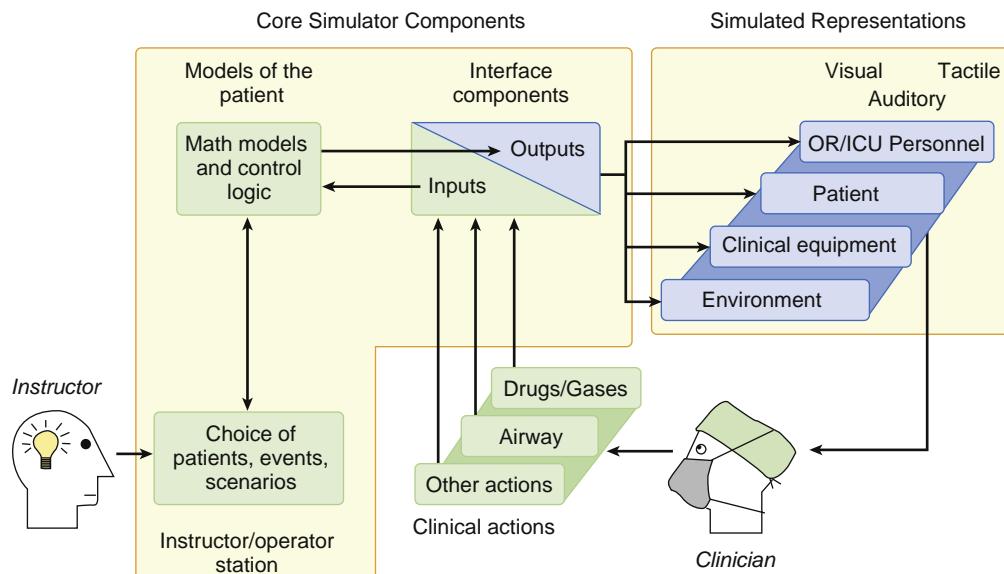
**Standardized patients.** Standardized patients (SPs; in some countries referred to as “simulated patients”) are actors/role players who are trained to represent a patient's condition (e.g., symptoms or social situation) and may be trained to score a participant's performance and to provide informative feedback. Over the last three decades, students increasingly learn skills in medical history taking and physical examinations using SPs.<sup>170</sup> Overviews of the use and implementation of SPs in anesthesia education are available.<sup>191-193</sup> SP-based simulations are increasingly being used for issues such as disclosure of bad news and other difficult conversation as well as in pain medicine.<sup>194</sup>

**Hybrid simulation.** Hybrid simulation means combining different types of simulation modalities during a simulation scenario. It can be used in different ways and serves several purposes: (1) *Pairing simulation devices in parallel*. This way, a training atmosphere can be established, in which different professions can have credible clinical work for their role. For example, when training the management of complications in the OR with surgeons and anesthesiologists together, it is helpful if both professions have clear functions during the scenario. For example, Kjellin et al. performed a multidisciplinary OR team training, where training was performed in a mock-up OR equipped with a mannequin-based patient simulator and a laparoscopic simulator.<sup>195</sup> Another option is to integrate manufactured life-like surgical models with the mannequin, as used by Weller et al. for multidisciplinary OR team training.<sup>14</sup> (2) *Pairing simulation devices in sequence*. This way, the best characteristics of each simulation modality can be used in a scenario and create a simulation that is more than the sum of the parts. For example, a scenario can start with a standardized patient/role player presenting in a patient bed or gurney; the simulation can be transferred to a mannequin at a critical point, such as when invasive activities are needed (e.g., intubation or CPR) or when giving birth. Cantrell and Deloney offer suggestions for integrating SPs into high-fidelity simulation scenarios.<sup>192</sup>

## Simulation Fidelity and Classification of Simulators

Simulation is becoming more commonly used for education and training purposes as well as for continuing professional development. But people often have very different perceptions of the definition of the term simulation. This highlights the need for definitions of simulation modalities, simulation fidelity, a classification of the relevant technologies and features, and also a brief overview about the methods of teaching.

**Simulation fidelity and simulator capability.** In the simulation literature the term fidelity—which means how closely something replicates reality—is often used to refer to specific devices or products. In contrast, the authors believe strongly that this is a misnomer and that the concept of fidelity is a property of the simulation *activity* and not primarily of the device(s) or



**Fig. 7.3 Schematic diagram of the generic architecture of patient simulator systems.** The simulator generates a representation of the patient and the work environment with appropriate interface hardware, display technologies, or both. The representation is perceived by the anesthesia professional, whose actions are input to the simulator through physical actions or input devices. The behavior of the simulated scenario is manipulated by the instructor or operator through a workstation that allows selection of different patients, abnormal events, and other features of the simulated patient. The control may be manual, script based, or model based with manual adaptation to reach optimal learning outcomes. *ICU*, Intensive care unit; *OR*, operating room. (Diagram by D.M. Gaba.)

products used. That is, fidelity is determined by the number of aspects that are replicated by the simulation (not only physical ones) and the applicable representation of each aspect relative to that of the real world (see subchapter on simulation realism). The fidelity required of a simulation depends on the stated goals and participant population. Some goals can be achieved with minimal and low fidelity, whereas others require very high fidelity.

**Classification of simulators.** For some purposes it is useful to compare the levels or specifics of the particular technological *capabilities* of simulator devices. There is no universally accepted classification scheme for describing simulators in anesthesia.<sup>169</sup> Any classification involves some overlapping and gray areas.<sup>159</sup> Cumin and Merry describe a classification that is based on the three pillars of (1) user interaction, (2) physiology base, and (3) use.<sup>196</sup> Gaba<sup>171</sup> classifies simulation modalities according to the following scheme: verbal simulation (i.e., “what-if” discussions, storytelling, trigger videos, role playing), SPs, part-task trainers (including realistic mock-up devices and tissue simulation), computer patient (i.e., VR simulation, microsimulators/screen-based simulators), and electronic patient.

In this chapter, a *patient simulator* (as opposed to a part-task trainer) is a system that presents an approximation of a whole patient (not only parts of it) and a clinical work environment of immediate relevance to anesthesiologists (e.g., operating room, postanesthesia care unit, ICU, etc.). A patient simulator system contains several components (Fig. 7.3).<sup>159</sup> Some of the currently available features of typical mannequin-based patient simulators are presented in Table 7.1.

In the following, the major education and teaching purposes of main simulator classifications are presented. The presentation is partly based on the idea of the Miller prism (also pyramid or triangle) of clinical competence. For a more elaborate overview the reader is referred to further literature.<sup>75</sup>

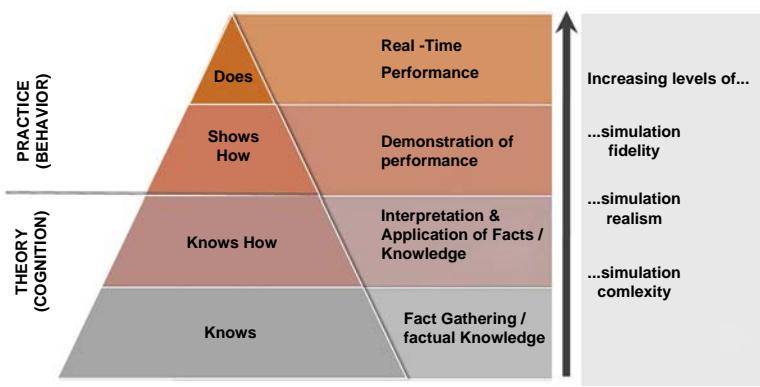
**Miller's learning pyramid.** For each simulation a variety of different learning objectives exist. Largely they can be aligned to the Miller pyramid<sup>197</sup> shown in Fig. 7.4. On the cognition level, simulations can be used to help learners acquire new knowledge and to better understand conceptual relations and dynamics (“knows,” “knows how”). For example, physiologic simulations allow students to watch cardiovascular and respiratory functions unfold over time and how they respond to interventions—in essence, bringing textbooks, diagrams, and graphs to life. The next step on the spectrum is acquisition of isolated skills to accompany knowledge (“knows how,” later “shows how”). Some skills follow swiftly from conceptual knowledge (e.g., cardiac auscultation) while others involve intricate and complex psychomotor activities (e.g., catheter placement or intubation). Isolated technical and non-technical skills must then be assembled into care processes and existing workflow concepts, creating a new layer of clinical practices (“shows how,” later “does”). Over time those assembled skills get integrated into practice and become part of daily performance (“does”). The expert health care professional performs only in the “does” triangle, except when honing old skills or learning new ones. However, there may be a gap between the level of performance that individuals—or teams or work units—“do” compared to the optimal level. Often, clinicians might be able to demonstrate

**TABLE 7.1** Functionality of Typical Current Mannequin-Based Simulator Systems\*

Clinical Area	Features and Functions	Remarks
Airway	Appropriate pharyngeal and glottic anatomy Placement of facemask, ETT, supraglottic airway devices, Combitube Laryngospasm, tongue and airway swelling, cervical immobility, jaw closure, breakable teeth Cricothyrotomy Transtracheal jet ventilation Bronchial anatomy (to the lobar bronchus level)	The airway often provides an acceptable seal for ETT; the seal for supraglottic airway devices can be variable, but it generally does allow positive pressure ventilation. The facemask seal is variable (plastic on plastic) Cricothyrotomy of modest anatomic realism; the tissue does not feel like real skin and lacks a subcutaneous fat layer; no bleeding occurs; however, the simulation does allow going through the physical steps of inserting a subglottic surgical airway.
Head	Eyelid movement, pupil dilation, and reaction to light or medications Patient voice and sounds such as coughing and vomiting (through built-in loudspeaker) Palpable carotid pulses Cyanosis represented by blue light at the edge of the mouth  Tearing, sweating	A live voice is preferred to the prerecorded audio clips because of higher flexibility in scenarios.  The blue light is a cue that the patient is cyanotic, but it does not physically replicate the appearance of cyanosis.
Chest	Physiologic and pathophysiologic heart and breath sounds Spontaneous breathing with chest wall movement  Bronchospasm Adjustable pulmonary compliance Adjustable airway resistance Pneumothorax Needle thoracotomy and chest tube placement  Defibrillation, transthoracic pacing ECG Chest compressions	Breath and heart sounds through loudspeakers; sounds contain artifacts and mechanical noise. Often sound level depends on position of stethoscope relative to loudspeaker.  As for cricothyrotomy the anatomy is not very realistic, but the mannequin may allow performance of these procedures.
Extremities	Palpable pulses (dependent on arterial pressure) Cuff blood pressure by auscultation, palpation, or oscillometry Modules for fractures and wound modules Intravenous line placement Thumb twitch in response to peripheral nerve stimulation Arm movement  Representations of tonic-clonic seizure activity	Most current simulators do not provide even limited robotic movement of limbs.  These representations are cues that lack anatomic reality.
Monitoring (waveforms or numeric readouts)	ECG (including abnormalities in morphology and rhythm) SpO <sub>2</sub>  Invasive blood pressure CVP, PAP, PCWP Cardiac output Temperature CO <sub>2</sub> (may be actual CO <sub>2</sub> exhalation) Anesthetic gases (may have actual uptake and distribution of agents) Cardiopulmonary bypass	Most simulators provide a simulated virtual vital signs display; some can interface to actual clinical monitors.  Some simulators include(d) a virtual cardiopulmonary bypass machine.
Automation and sensors	Chest compressions Ventilation rate and volume Defibrillation and pacing (including energy measurement) Gas analyzer (inspired O <sub>2</sub> , anesthetics) Drug recognition (drug identification and amount)	

CO<sub>2</sub>, Carbon monoxide; CVP, central venous pressure; ECG, electrocardiogram; ETT, endotracheal tube; O<sub>2</sub>, oxygen; PAP, positive airway pressure; PCWP, pulmonary capillary wedge pressure; SpO<sub>2</sub>, saturation of peripheral oxygen.

\*The features listed are each present in some existing simulators, but not all features are present on any single device. Sets of features depend on the device and model.



**Fig. 7.4 Miller's learning pyramid, also known as Miller's prism of clinical competence.**<sup>197</sup> Based on the Miller's learning pyramid, the clinical competence of an anesthesia professional is built on four different competence levels, that can be divided into theory (a person's cognition: "knows" - "knows how") and practice (a person's behavior: "shows how" - "does"). The most relevant clinical competence is the real time performance ("does"). Those four levels need to be considered when addressing learning goals as well as assessment goals of simulation. The figure is modified from a publication of Alinier,<sup>368</sup> indicating that simulation fidelity, simulation realism, and simulation complexity increase with different levels of competency.

"knows how"—"shows how" without necessarily being able to "do" under all relevant circumstances and occasions. Simulation can be a valuable tool to close such gaps.

#### PATIENT SIMULATION ACTION BOX

In the current health care system, for most invasive procedures, novices' first time performing a task is on a real patient, albeit under supervision, and similarly they will then climb the learning curve by working on real patients. Simulation offers the possibility of having novices practice both before their apprenticeship-like work as well as honing those skills with simulation in parallel with their clinical experiences. This is especially useful because simulation lets them gain experience even with uncommon anatomic or clinical presentations.

**Non-technological simulation.** Verbal simulations ("what-if" discussions), storytelling, paper and pencil exercises, and experiences with SPs require little or no technology, but can effectively evoke or recreate challenging clinical situations. Similarly, even pieces of fruit or simple dolls can be used for training in some manual tasks. Some education and training on teamwork can be accomplished with role playing or discussion of videos of relevant events.

**(Computer) Screen-based simulators (microsimulators)** that present the patient on the screen as drawings, photos, or videos, while allowing clinical actions or changes to be chosen can be used to teach basic concepts and technical material, such as the uptake and distribution of inhaled anesthetics or the pharmacokinetics of intravenous drugs. Such programs are inexpensive and easy to use. They allow the presentation of and practice with the concepts and procedures involved in managing normal and abnormal case situations,

mostly targeting the parts of the Miller pyramid referred to as "knows" and "knows how," commonly for early learners.

**Part-task trainers** include artificial (and occasionally animal or human cadaver) models used to teach particular procedural skills, for example intubation, intravenous or intraosseous access, regional anesthesia techniques, thoracic drainage, and use of difficult airway management devices. These target "knows how" and "shows how." Such trainers are most commonly used with novices having little experience with the procedure, or to retrain experienced personnel in the application of the particular tools.

**Mannequin-based simulators**, representing most or all of a patient, can be used to capture the full complexity of the real task domain, including application of clinical skills and clinical algorithms in combination with human-machine interactions and the complications of working with multiple personnel. They can be used to address "shows how" extending into "does," at least in simulation (see later section on translational research levels). Therefore, MBS are appropriate to teach diagnosis and management of challenging situations as well as non-technical skills and human-factor-based behavior (see [Chapter 6](#)). These can be used, with different educational approaches, for all levels of learners. For early learners it is common to use a teacher in the room as an advisor or coach, and to control the simulation by "pause and reflect" allowing the scenario to be stopped and continued or restarted as necessary to maximize their learning.

#### PATIENT SIMULATION ACTION BOX

Compare to Miller's learning pyramid: If participants are not (yet) familiar with the clinical concepts, procedures, or tasks needed for the mannequin-based training, they should usually be taught those in other ways prior to full-scale simulation.

**TABLE 7.2** Site of Simulation and the Related Advantages and Disadvantages

Site of Simulation	Advantages	Disadvantages
Dedicated center ( <i>fixed facility not part of an actual clinical work unit</i> )	<ul style="list-style-type: none"> <li>■ Equipment permanently installed, minimized setup time, high level of control and infrastructure</li> <li>■ Facilitated use of complex audiovisual systems</li> <li>■ Facilitated conduct of detailed debriefing of simulation involving video review</li> <li>■ Ease of scheduling</li> <li>■ No interference with actual clinical work, protects personnel from being pulled into real clinical work</li> <li>■ Multipurpose use</li> </ul>	<ul style="list-style-type: none"> <li>■ Inability to recreate exact work unit, equipment, supplies of diverse target populations</li> <li>■ Possible difficulties for clinicians to be off duty to attend training</li> <li>■ Personnel not readily available for clinical work</li> <li>■ Eventually remote from site of clinical work</li> <li>■ Creating and maintaining a dedicated simulation center is expensive</li> <li>■ Does not probe actual clinical setting</li> </ul>
■ Temporary in situ simulation ( <i>Actual work unit; temporary setup and takedown</i> )	<ul style="list-style-type: none"> <li>■ Real clinical site</li> <li>■ Probing/training of personnel in their actual work unit, using real equipment/supplies</li> <li>■ Ready ability for clinicians to attend in proximity to their work</li> <li>■ Probes actual clinical site(s) and system(s)</li> <li>■ Less expensive than operating a dedicated simulation center</li> </ul>	<ul style="list-style-type: none"> <li>■ Vacant clinical space is not always available</li> <li>■ Difficulties in scheduling—may need site for clinical use</li> <li>■ Possible interference with actual clinical work; personnel readily drafted to return to clinical work</li> <li>■ Distractions from onlookers is hard to control</li> <li>■ Minimal audiovisual system, less audio-video recording capability</li> <li>■ Great effort of setup and takedown</li> </ul>
■ Residential in situ simulation ( <i>Actual work unit; permanent facility</i> )	<ul style="list-style-type: none"> <li>■ Same as temporary in situ</li> <li>■ Minimized setup time</li> <li>■ Complex audio-video system available</li> <li>■ Easy scheduling</li> </ul>	<ul style="list-style-type: none"> <li>■ High cost of creating a permanent simulation bed in a clinical work unit</li> <li>■ Possible interference with actual clinical work; personnel readily drafted to return to clinical work</li> <li>■ Distractions from onlookers is hard to control</li> </ul>
■ Peri-situ/off-site simulation ( <i>simulation in a nonclinical environment such as a conference room, etc.</i> )	<ul style="list-style-type: none"> <li>■ Good to schedule</li> <li>■ Simulation can be used without clinical space or a dedicated simulation center needed</li> <li>■ Every training is better than no training</li> <li>■ Many supplies and some equipment can be used as if it was the real thing</li> </ul>	<ul style="list-style-type: none"> <li>■ Lack of ideal realism of bedside or in situ training</li> <li>■ Minimal audiovisual system, less audio-video recording capability</li> <li>■ Great effort of setup and takedown</li> <li>■ No system probing</li> </ul>
■ Sequential location simulation/“moving simulation” ( <i>simulated transport of simulator from site to site</i> )	<ul style="list-style-type: none"> <li>■ The challenging clinical work of transport itself</li> <li>■ Replication of natural flow of patients and hand-offs between teams</li> </ul>	<ul style="list-style-type: none"> <li>■ Requirement for multiple simulation sites</li> <li>■ Technologic limitations of portable wireless simulators</li> <li>■ Great effort of setup and takedown</li> </ul>
■ Mobile simulation ( <i>travel of simulation systems and instructor crew to client or neutral sites</i> )	<ul style="list-style-type: none"> <li>■ Simulation expertise brought to those who cannot or wish not to invest in it themselves</li> <li>■ For in situ use, all advantages thereof</li> </ul>	<ul style="list-style-type: none"> <li>■ Possibly high transport costs (driver, fuel, vehicle)</li> <li>■ For in situ use, all disadvantages thereof plus even greater effort for setup and takedown</li> </ul>

#### PATIENT SIMULATION ACTION BOX

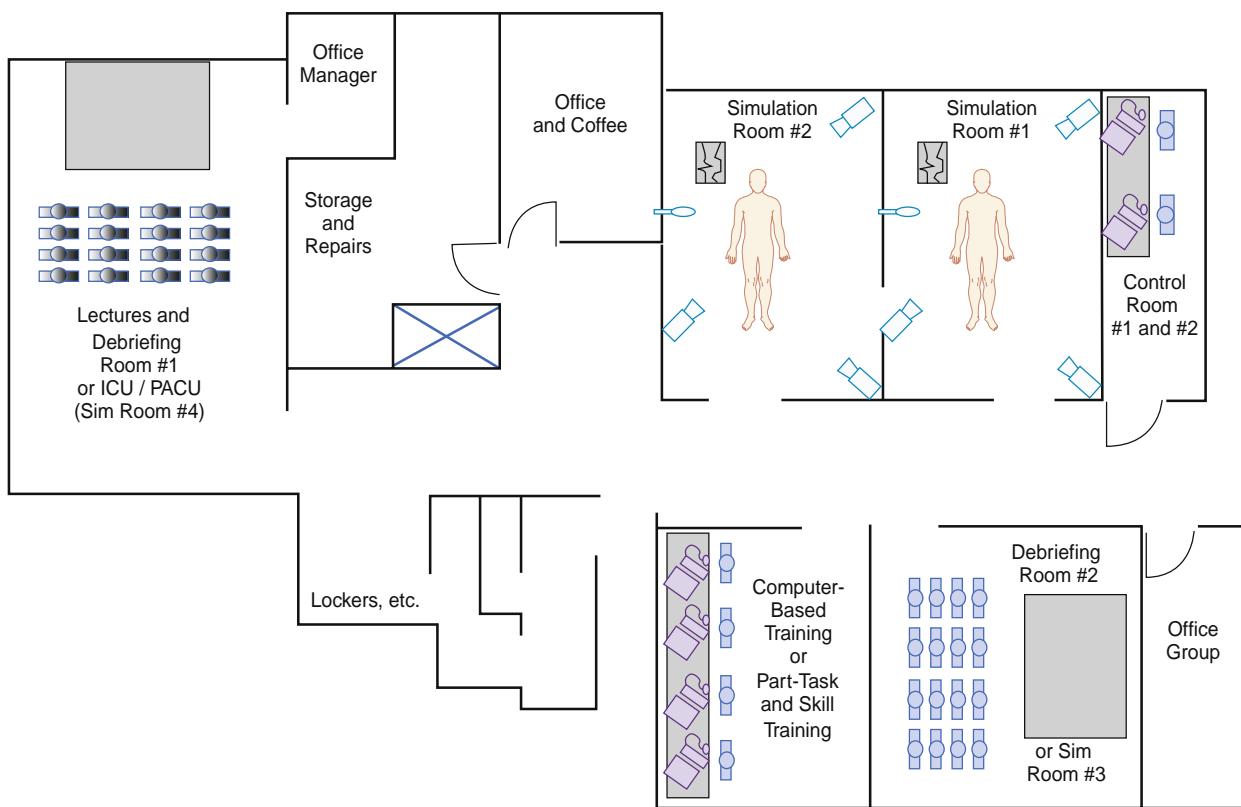
Regardless of the device used, the simulator is only a teaching tool that must be coupled with an effective curriculum for its use.<sup>198</sup> The more complex simulations get (i.e., MBS) and the more a simulator represents a whole patient—to be treated by one or more teams—the more it is important to have qualified instructors with special training.<sup>198</sup>

## Sites of Simulation

Some types of simulation such as nontechnological ones and those that use videos or computer programs can be conducted in the privacy of the learners' home or office using their own equipment. Part-task trainers and mannequin-based simulation are often used in a dedicated

simulation center, but MBS is increasingly also done “in situ” (in place)—in a real patient room/bed—or “peri-situ” (near the place)—nearby elsewhere in the clinical work unit. For large-scale simulations (e.g., disaster drills<sup>49,86</sup>), the entire organization becomes the site of training, or in the case of a “moving” simulation, different parts of an organization become the site of training. If the simulation training takes place outside the organization, but uses the equipment and personnel of the organization, it is called “mobile” simulation.

Often simulation personnel that work in a dedicated center may either also conduct simulations “in situ,” “peri-situ,” “mobile,” and “moving patients exercises” or may mentor others who do so. The advantages and disadvantages of different simulation sites are discussed in each respective section and summarized in Table 7.2. Sørensen and associates give an overview of the advantages and disadvantages of different simulation sites in a recent publication in 2017.<sup>199</sup>



**Fig. 7.5 Simulation Center Floor Plan.** An intermediate-sized simulation center with four simulation rooms (sim room), a computer-based training room, and several multipurpose rooms, equipped with audio-video patch panels to adjust the room use flexibly to the needs of different training activities (e.g., the large seminar room can be used as a large intensive care unit [ICU] or postanesthesia care unit [PACU]). (Figure by M. Rall & E. Stricker, Center for Patient Safety and Simulation [TuPASS], Tübingen, Germany.)

## DEDICATED SIMULATION CENTER

Many institutions have chosen to construct one or more complete simulation centers in which to conduct a variety of education and training sessions. At a few places entire “simulation hospitals” have been created (e.g., Miami, <https://simhospital.sonhs.miami.edu/>). Some useful websites of simulation centers and other resources are listed at the end of the chapter (Appendix 7.1). The cost structure of a simulation center is a complex issue (see later subchapter). But these programs and their managers in charge have already voted with their feet on the issue of cost versus benefit.

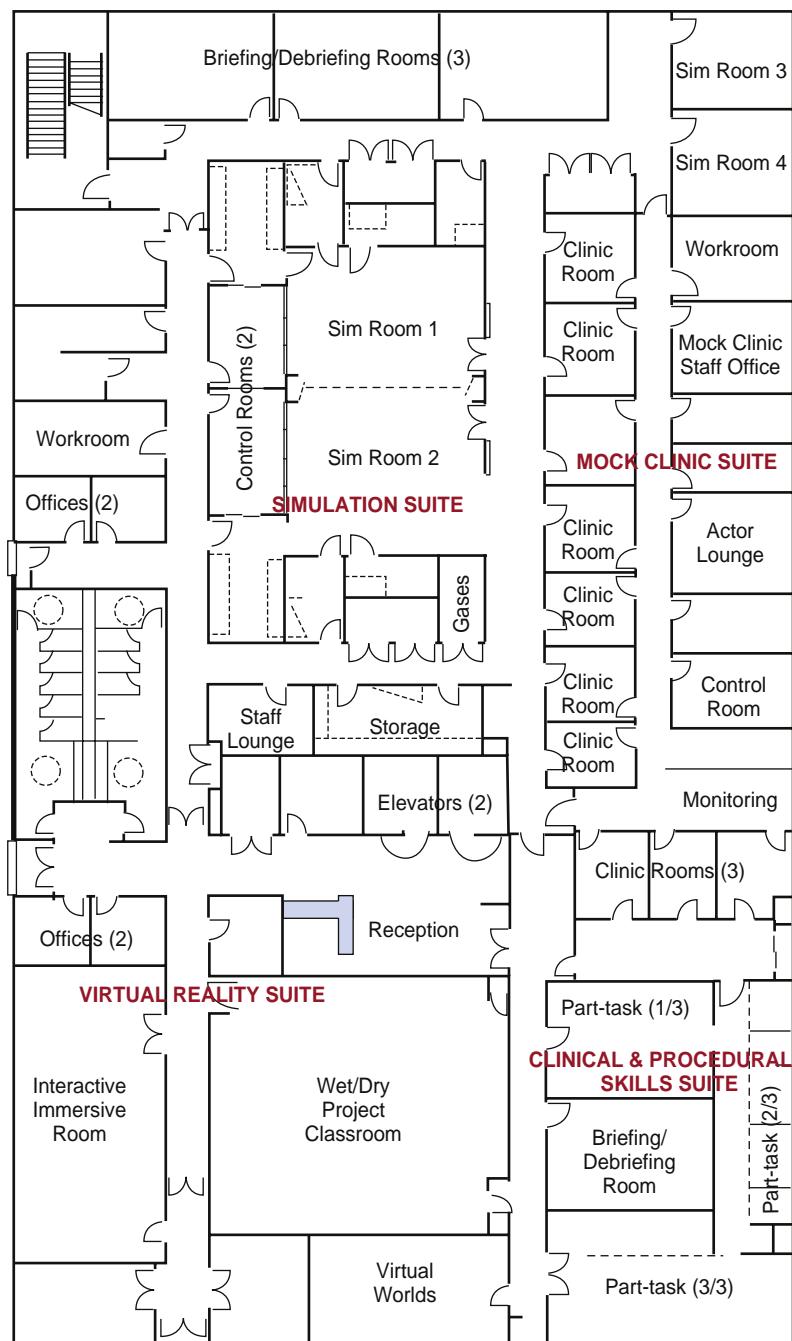
In a dedicated simulation center, one or more simulators may be used, typically in rooms that partially or fully replicate, in a relatively generic fashion, various clinical environments (e.g., operating room, ICU, labor and delivery, emergency department, etc.). Fig. 7.5 and Fig. 7.6 show the floorplan of a medium-sized and a large simulation center. Fig. 7.6 shows the floor plan of the Immersive Learning Center at Stanford University, a pioneering center for health care simulation.

Typically, simulation centers provide a separate control room to allow complex simulations to be presented without an instructor intruding on the simulated case. Fig. 7.7 shows a simulation control room. Many simulation centers have audio-video systems allowing the recording of multiple views during patient simulation. Some centers have computer-based systems to allow annotation of video on the fly and rapid search to the marked portions, but others

have found that such mechanisms are not necessary to support debriefing. Dedicated centers typically provide one or more debriefing rooms, often with video replay capability. Ideally a center is located to be easily accessible to a variety of participant populations. Designing, equipping, and overseeing construction of a simulation center may benefit from special knowledge or prior experience.<sup>200,201</sup>

Universities and hospitals or hospital networks are increasingly constructing very large multidisciplinary and multimodal simulation facilities that often still have anesthesiologists in leadership positions. Often, these kind of facilities combine all the types of simulation and immersive learning in one large unit, including actors playing SPs (usually in clinic settings), mannequin-based simulation, part-task and surgical and procedural trainers, wet and dry work (e.g., plaster casting or procedures on food products), and different forms of VR. Sometimes these incorporate facilities for dissection of cadavers or the use of anesthetized animals but often these are in other pre-existing sites. Some institutions have many simulation centers, associated with different learner populations, in different locales, or featuring different kinds of simulation equipment.

**Advantages and Disadvantages of Dedicated Simulation Centers.** Simulation in a dedicated center facilitates scheduled training and allows the use of complex audiovisual gear and a variety of simulation and clinical equipment, with substantial storage. Devices can be preset, tested, and



**Fig. 7.6 Simulation Center Floor Plan.** Floor plan of a large interdisciplinary simulation center for multiple domains (anesthesia, surgery, students) with several multipurpose simulation rooms (sim room) and skills laboratories. (Figure by D. M. Gaba at the Immersive Learning Center at the Stanford School of Medicine, Stanford, California.)

ready to go, with briefing and debriefing facilities immediately at hand. In a dedicated center inexpensive discarded, flawed, or outdated clinical equipment and supplies can be safely used. When a center incorporates all modalities of simulation in one place it fosters hybrid techniques, as when an actor playing a standardized patient is combined with a part-task trainer, or when a surgical simulator is combined with a mannequin-based patient simulator.

The main disadvantage of a dedicated center is its cost of construction and outfitting. Moreover, no matter how well equipped it is, it can never replicate the equipment,

layout, and clinical processes of any specific clinical workplace. Also, participants know from the very beginning that the activity is a simulation and not the real thing.

### TRAINING AND PROBING WHERE CLINICIANS WORK

There are several approaches to conducting simulations in or near actual sites of clinical work. By necessity institutions without a dedicated simulation center must use one of these approaches, but they are useful for many other reasons.



**Fig. 7.7 Simulation control room.** Through a window wall the simulation control room is separated from the actual simulation room. Several instructors can have a look on the simulation either via the windows, or via one of the several screens that show different views of the simulation room. In front of the instructors the workstation for control of the simulator system itself is placed, including an audio control desk with control of the simulated patient voice, the voice for in-scenario guiding, and several wireless headset channels. (Photograph provided by D.M. Gab; control room of the Stanford Immersive Learning Center.)



**Fig. 7.8 In situ mobile simulation in a catheterization laboratory (cath lab).** The simulator is placed on the cath lab table, surrounded by the x-ray equipment, thus complicating treatment of the patient by limiting space. The vital signs monitor provides relevant data to the clinical team. The simulator is controlled from the cath lab control room. Multiple mobile cameras and a scan converter for vital signs provide a live video transmission to a temporary debriefing area for the nonactive part of the training group and allows for crisis resource management-based debriefings. (Photograph by M. Rall.)

## In Situ Simulation

*In situ simulation* is conducted in an actual bed/gurney/bay of a real clinical workplace, such as, for example, OR, ICU, trauma room, postanesthesia unit, or ward. ISS training is often used for complex patient simulation scenarios with experienced single-discipline or interprofessional staff. It is typically used for training in order to create high environmental fidelity and/or to probe procedures or the system (see earlier subchapter “Application of Simulation”).<sup>4,75,83-87,202</sup> ISS can be a useful training option especially for training in unique workplaces that are difficult to recreate with adequate realism (see later subchapter on simulation realism) in a simulation center or elsewhere, such as a catheterization laboratory, a CT scanner, an ambulance, or an air rescue aircraft (Figs. 7.8 to 7.15).

Rosen and colleagues<sup>203</sup> reviewed the use of in situ simulation in the continuing education for health care professions. They summarized that a positive impact of ISS on learning and organizational performance has been demonstrated in a small number of studies. They also indicated that the evidence surrounding ISS efficacy is still emerging and that existing research is promising.

Most ISS is performed mobile as a temporary setup only for the training sessions. In very few institutions a simulator is permanently installed in a clinical workplace, for example, creating a simulation-specific patient room in the actual ICU.

**Advantages and Disadvantages of In Situ Simulation.** ISS seems ideal in that it probes and challenges personnel and systems as they actually exist, thus unmasking real issues of patient care. It is available, in principle, to all sites, even those without a dedicated center, and it is conducive to short courses and unannounced mock event drills.

Because it takes place in the actual work unit, it will eliminate travel time to a dedicated center and will put participants at ease. Some substantial disadvantages include potential distractions by ongoing clinical work, lack of privacy, logistics of setup and takedown, reduced availability of



**Fig. 7.9 In situ mobile simulation in a dentist chair.** The simulator was equipped with artificial teeth, gum and a chalk tooth to drill, thereby simulating the dentist's procedures. Then emergencies developed, allowing the team to respond. Training focused on crisis resource management key points and medical aspects including use of an automated external defibrillator. (Photograph by M. Rall.)

AV and simulation equipment, and supply costs (many ISS activities use the unit's real clinical supplies as needed).<sup>204</sup> ISS can be difficult to organize, schedule, and control. The clinical area planned for simulation may not be vacant or may be needed on short notice. Staff members engaged in the simulation are prone to being pulled into clinical duty, and training sessions may be interrupted. Raemer<sup>204</sup> summarized potential risks of ISS and amplified some of the safety hazards of simulation itself including maintaining control of simulated medications and equipment, limiting the use of valuable hospital resources, preventing incorrect learning from simulation shortcuts, and profoundly upsetting patients and their families. In our experience, patients and families are rarely upset and in fact often are pleased to see that such serious training is going on.



**Fig. 7.10 In situ mobile simulation team training in the operating room (OR).** The mobile simulation control room is set up outside the OR. The instructors can watch the simulation scenario either indirectly via live video coverage (left photo) or directly via the OR window (right photo). (Photograph provided by M. Rall, InPASS in situ training in the OR at Scuol Hospital, Switzerland, Chairman: J. Koppenberg.)



**Fig. 7.11 In situ mobile simulation team training in a medical air rescue helicopter.** The mobile simulation control room with several cameras and microphones is set up outside the helicopter and provides a multi-perspective view inside to monitor the scenario and react to activities performed. (Photograph taken by M. Rall at Aimed 2008 with the German Air Rescue (DRF) team.)



**Fig. 7.12 In situ mobile simulation trauma team training at a large trauma center.** (Photo provided by M. Rall.)

### Peri-situ or Off-site Simulation

If simulation is, in principle, worthwhile, then doing simulation anywhere is probably better than not doing it at all. *Peri-situ simulation* (PSS) means simulating in the clinical work unit, but not in an actual patient room/bay/bed—for example in a conference room, or even hallway of the unit. This may be done when an ISS session is planned but there is no actual clinical spot available, or it may be done this way on purpose. PSS has some of the advantages of ISS in terms of locale, systems, and supplies, but it lacks the ideal realism of an actual bedside. When simulation is done outside a clinical unit (say a nonclinical conference room) or in a public area of a hospital it is referred to as *off-site simulation* (OSS).

### Sequential Location Simulation

This is sometimes called *moving simulation* and it simulates the patient moving between different sites of care in one scenario, at each stop enacting what might transpire in that location. For example, the patient could be brought to the emergency department by ambulance; assessed and treated; then taken to CT scan, interventional radiology, or OR; and finally transferred to an ICU. Moving simulation may be best accomplished as ISS or PSS, but again, there will be some value to it even if each stop cannot be simulated perfectly. To do it with full veracity requires intensive coordination and complex choreography of simulation equipment and personnel. It is probably only worth it if done occasionally and primarily with a focus on systems probing and improvement. Moving simulations can address different specific issues at each stop, depending on the most important systems probing and learning issues for each.

**Advantages and Disadvantages of Moving Simulation.** Like all kinds of ISS, moving simulation is a powerful tool to detect latent threats in the system. Apart from a focus on latent threats in certain workspaces, this kind of ISS can detect challenges in the course of transport to those workspaces. As mentioned above, the organizational and technical preparations, the technical challenges, and the movement of the whole simulation gear paired with the clinical staff needed in order to make moving simulations work imply huge effort.



**Fig. 7.13 In situ mobile simulation in an intensive care unit (ICU)/intermediate medical care unit location.** The training in clinical areas is especially useful for ICU-like surroundings. Crisis resource management-based trainings showcase these highly complex problems and the interactions needed to coordinate high-performing ICU teams. The training allows for checking the local arrangement of equipment and the readiness to react to certain emergencies. There are already a few examples of permanent in situ simulation facilities in ICUs (see text). (Photograph by M. Rall.)



**Fig. 7.15 Neonatal crisis resource management and resuscitation training at a neonatal emergency workplace.** The experienced instructor (on the right side of the infant) is a confederate acting as part as the team, whereas others in the control room preside over simulation. (Photograph taken at Stanford Simulation Center, Stanford University, Palo Alto, California; provided by M. Rall.)



**Fig. 7.14 In situ mobile crisis resource management (CRM)-focused simulation team training inside an operating room.** This debriefing room is temporarily set up in an induction room. The use of videos for debriefing (here on a 42-inch flat panel placed over the basin) is feasible even in this setting. Training inside a hospital often includes training actual teams with the same setup, if possible conducting training for a large proportion of the relevant personnel. "En-bloc" training sessions may have a greater impact and longer-lasting effects of the lessons learned, including CRM behaviors. (Photograph by team TuPASS [Center for Patient Safety and Simulation, University Hospital, Tübingen, Germany], who performed a full team training of the anesthesia department at Steinenberg Medical Center, Reutlingen, Germany.)

## MOBILE SIMULATION: "HAVE SIMULATOR, WILL TRAVEL"

Mobile simulation means that the simulator and the audiovisual gear are transported outside the originating institution for purposes of a simulation event. This makes simulation activities an option for clinical sites that lack a dedicated

simulation center or the expertise to do ISS/PSS in their own institution.

Mobile simulation can be conducted in clinical settings or in conference rooms, or even hotel meeting rooms. Mobile simulation can be provided by staff from simulation centers that have mobile simulator and audiovisual equipment and are equipped to travel with it. In some places there are small simulation centers built into a truck or bus.

**Advantages and Disadvantages of Mobile Simulation.** For clients who use mobile simulation, the construct of mobile simulation for sure is a great way to know the promise of simulation training and system probing without extra time and money for staff travelling. At the same time, mobile simulation offers the advantage of external peer feedback. This way normalizations of deviance (see [Chapter 6](#)) and pitfalls that are not noticed by internal personnel anymore can be detected by external instructors. Organizations that offer mobile simulation show a greater flexibility for training opportunities. Such organizations can not only offer training at nearly any workspace in their own organization, but also offer simulation to other organizations. This way, the organization's own simulation activities might be funded and vacant equipment and personnel capacities used.

## Simulation Team Training Participants: Who Should Be Trained and in What Composition?

Each discipline in health care can be considered a *crew* containing one or more individuals. Several crews may work together closely as a *team*. The operating room team, for example, consists of an anesthesia crew, a surgery crew, and a nursing crew (and crews of technicians and support personnel). The members within a crew are likely to be more familiar with each other than with members of other

crews. Such mutual professional (and private) “knowing about each other”—perhaps by enhancing their shared mental model—could be an important influence on their performance.<sup>205</sup>

Many simulation applications are targeted at individuals. These may be especially useful for teaching knowledge and basic skills or for practice on specific psychomotor tasks. As in other high-reliability industries (including anesthesiology, see [Chapter 6](#)), individual skill is a fundamental building block, but empiric findings show that individual performance is not sufficient to achieve optimal overall performance, and to achieve optimal safety.<sup>206</sup> Performance and safety unfold in the interplay between people and in their interaction with each other, equipment, and organizational structures and processes. That is the reason why in high-reliability organizations a considerable emphasis is applied at higher organizational levels, in various forms of teamwork and communication training, and interpersonal relations. This approach is often summarized under the rubric of *crisis resource management* (see [Chapter 6](#) and later section).<sup>24,207,208</sup> The importance of teamwork and team training is widely accepted in health care and anesthesia,<sup>33,209-216</sup> although team training is still not widely implemented. The prerequisites for effective teamwork (e.g., team leadership, mutual performance monitoring, back-up and speak-up behavior, adaptability and team orientation, the concept of team cognition, etc.) are discussed in [Chapter 6](#). One of the special features of health care teams that poses several challenges is the frequently changing composition of teams with changing crews. Within a discipline, crew membership may fluctuate. For example, in anesthesia or the resuscitation team. Those teams or crews are also referred to as “action teams” (see [Chapter 6](#)).

When simulation is intended to go beyond specific medical and technical skills for individuals (as, for example, in CRM-oriented patient simulation) and to involve non-technical skills and teamwork, one can distinguish between single-discipline and multidiscipline approaches. CRM-based “team training” may be addressed first to *crews* (known as *single-discipline teams*), and then to *teams* (known as *multi-discipline teams*).<sup>217</sup> Commonly, in a broader sense and used this way in this chapter, the term “team training” refers to both single-discipline as well as multidiscipline training. For both approaches the best way to train and transfer learning for everyday instances at work is to arrange the training (1) interprofessional (doctors, nurses, allied health personnel, etc.) and (2) in realistic crew/team compositions and roles in regard to the learning objective (“train as you work”—see patient simulation action box below).

#### PATIENT SIMULATION ACTION BOX

“Train as you work.” When conducting patient simulation training with more experienced personnel—beyond “early learners”—those who work together should train together when possible. Although built on a foundation of previous experience and crew-specific training, working together in simulation will hone the skills of coordinating tasks, goals, and strategies in the overall treatment of the patient.

Furthermore, teams exist in actual *work units* in an organization (e.g., a specific ICU), each of which can be its own target for training, and in *organizations* as a whole (e.g., entire

hospitals or networks). Each unit can have specific characteristics, culture, etc., that will influence how receptive participants are for training and how easily they can apply in the clinical setting what they learned during simulation. Growing interest and experience have been shown in applying simulation to nonclinical personnel and work units in health care organizations (e.g., to managers, executives, informal leaders).<sup>73,74</sup>

Addressing teamwork in the single-discipline approach in contrast to the multidiscipline approach has advantages and disadvantages.<sup>155</sup> For maximal benefit, these approaches are used in a complementary fashion.

## TRAINING INDIVIDUALS

Simulation-based training of individual skills can be used to educate learners (Miller learning pyramid “knows,” “knows how,” see [Fig. 7.4](#)), to promote psychomotor skills (“knows how,” “shows how”), and to help integrate different kinds of skills into an effective whole. Usually, early learners need to start somewhere, as do experienced people trying to learn completely new skills or procedures. Whereas screen-based simulators can be used for educational purposes and the acquisition of basic procedural knowledge, part-task trainers promote psychomotor skills, and mannequin-based simulation allows training to bring different concepts together. When mannequin-based simulation is used for the training of individuals (who still perform as a crew!), the focus of patient simulation training lies either (1) on training an individual’s clinical skills, for example following a treatment algorithm; or (2) on training non-technical skills such as leadership, communication, task management, etc.; or (3) both.

## TRAINING CREWS: INTERPROFESSIONAL SINGLE-DISCIPLINE TEAM TRAINING

Training for crews (e.g., anesthesiologists) involves simulation scenarios, in which all participants are from a single discipline and in which the scenarios are highly relevant to the crew (both in regard to clinical and non-technical skills). The other team members’ roles (i.e., surgeons, etc.) are either played by instructor personnel or clinically savvy actors; less critical team roles may be played by participants or, when necessary, not present at all. In this approach the interaction with specific types of behaviors by other crew or team members can be addressed by an instructor or an actor assuming that role as a confederate. These roles can be designed such that participants can be exposed to different kinds of challenges systematically.

This approach allows tailoring simulations to challenge skills, knowledge, and situations specific to the discipline, including material that may be of little relevance to other members of the team and in the context of a wide variety of clinical situations (e.g., cardiac, orthopedic, or general surgery; labor and delivery; intensive care). Single-discipline training can emphasize generic skills of dynamic decision making, resource management, leadership, and teamwork applicable to any challenging clinical situation that is relevant to the particular discipline.

The single-discipline approach may be of particular relevance and value for professionals who work in many different settings and who do not work in permanent crews or teams (“action teams,” such as in anesthesia, see [Chapter 6](#)), and

who therefore must acquire generic teamwork and communication skills that can be used with all co-workers. For dedicated center simulations, single-discipline sessions are simpler logically because only one discipline needs to be present, rather than scheduling someone from each of the disciplines.

## TRAINING TEAMS: INTERPROFESSIONAL MULTIDISCIPLINE TEAM TRAINING

In health care, interdisciplinary teams are becoming ubiquitous. At the same time, experts from each discipline do not necessarily combine to make an expert team.<sup>218</sup> The complementary approach is to conduct *multidiscipline team training* (also called *combined team training* or *interprofessional training [IPE]*). Here, the crews of different disciplines who might work together undergo training together, each acting in their own usual roles, and scenarios designed to challenge all of the disciplines. Multidiscipline team training allows for more natural team interactions and reinforces understanding across the disciplines. Successful examples of such undertakings have been reported in many fields where anesthesia professionals are involved, including the OR,<sup>159,219</sup> obstetrics<sup>220-222</sup> (combining obstetrics, anesthesia, nursing, and neonatology and pediatrics), intensive care (combining physicians from multiple disciplines with nursing, respiratory therapy, and pharmacy),<sup>223</sup> emergency department,<sup>224,225</sup> and trauma management.<sup>30,31,90,226,227</sup>

Depending on the training location (see earlier subchapter), the scheduling of the team training poses several challenges. Multidiscipline training, for example, can be difficult to schedule in a dedicated simulation center. Ideally, the sessions will have instructors from several disciplines especially to handle debriefing. Multidiscipline trainings are typically easier to organize as *in situ* trainings (see earlier subchapter), or as announced or unannounced “mock events” (see next subchapter) that activate the actual designated team (e.g., ward or unit team, rapid response team, or code team). In the latter situation, the team does not know it is a simulation until they arrive at the scene.

## CROSS TRAINING: CHANGING ROLES

The course director of a simulation activity can choose whether to have all participants act in their own regular role, or to assume a different role. Each has its advantages. The philosophy of “train as you work and work as you train” would usually put everyone in their usual role,<sup>82</sup> but cross-training can provide an understanding of and sensitivity to the tasks, decision making, challenges, and responsibilities of another profession or discipline. Study results indicate that cross-training is an important determinant of effective teamwork process, communication, and performance,<sup>228</sup> enhanced shared team-interaction and mental models,<sup>229</sup> and helps to maintain team communication when faced with increased task demands.<sup>230</sup>

### PATIENT SIMULATION ACTION BOX

If a cross-training scenario is conducted it is advisable to brief personnel to represent the other professional role in a rational manner without playing out particular personality quirks or go “over the top.” The debriefing should emphasize discussion on what individuals can learn from “walking in some-

one else’s shoes.” It would be foolish, for example, to debrief anesthesia professionals on their surgical skills or behavior as a surgeon. Acting out may be fun for play but it is disrespectful to others, and wastes valuable simulation time.

## EN-BLOC TRAINING: AVOIDING SUB-THRESHOLD TRAINING EFFECTS

If patient simulation is used as an intervention to promote a patient safety initiative, for example the introduction of crisis resource management (see [Chapter 6](#)) to crews or teams, or the implementation of a new checklist, algorithm, etc., the organization/curriculum designer may arrange that all crew and team members are trained within a short period of time (i.e. several days or weeks). This would provide a more concentrated and uniform result. On the other hand, this may not be possible logically or politically within the institution, and may or may not be worth the “political capital” to make it happen. As there are no data to demonstrate the strength of the en-bloc effect, it is necessary to gauge under what circumstances it is worth the effort.

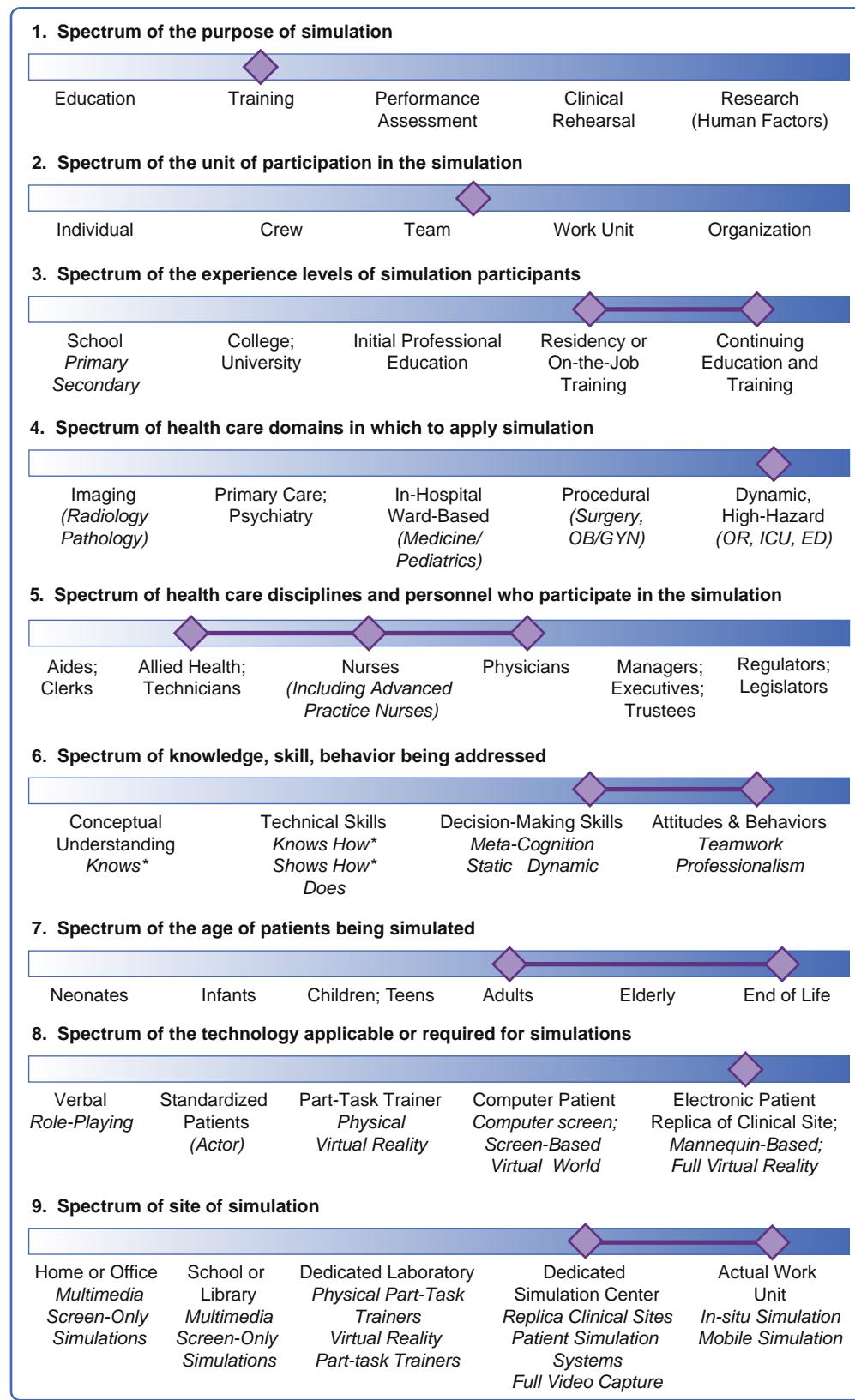
## Patient Simulation Timing: Announced in Advance Versus Unannounced in Advance

Regardless of site, simulations can be conducted as pre-scheduled exercises either for personnel in their regular-duty roles or for personnel on off-duty or education days. Typically, unannounced mock events (announced as if the real thing) would be implemented in a department after making potential participants aware of this possibility on a general level. Again, scheduled and unscheduled ISSs are complementary approaches, each with its own pros and cons. An obvious challenge is that it takes participants away from their actual patient care activities so that ground rules need to be established concerning when and how to abort the exercise when necessary. On the other hand, when done only occasionally and with appropriate safeguards, the clinical system needs to probe its ability to ensure good patient care when an emergency team is called to an event. In summary, the technique has high potential for organizational learning when done carefully.

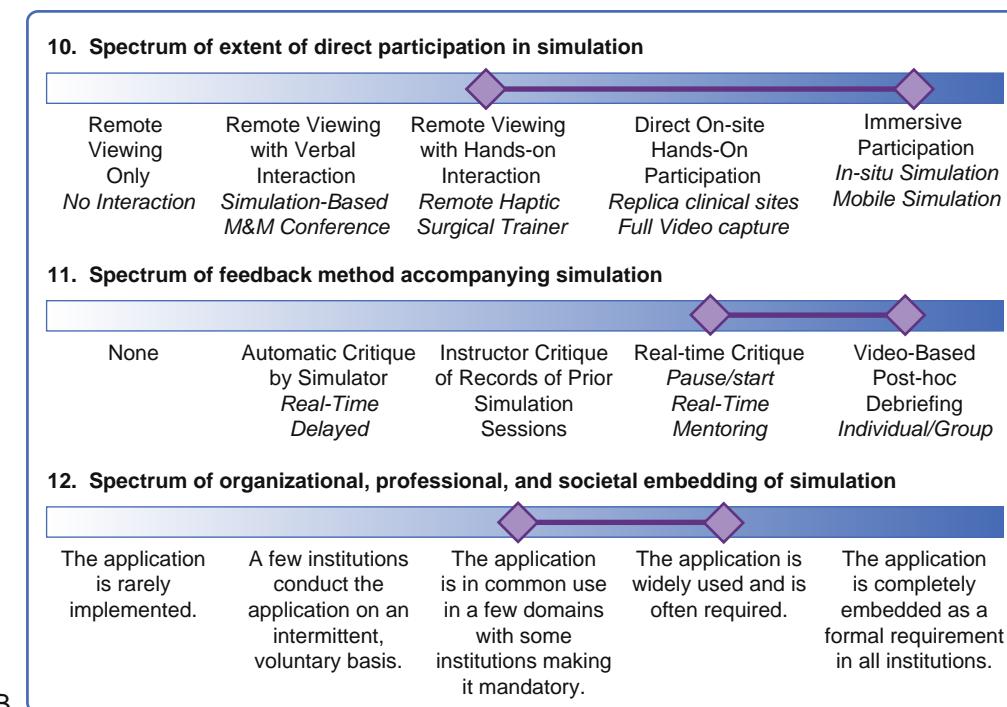
A number of recent publications discuss the advantages and disadvantages of unannounced mock events as well as issues concerning the implementation of such programs.<sup>199,231-233</sup>

## Scopes of Simulation in Health Care: The 12 Dimensions of Simulation

Many different aspects and variations of simulation have been presented so far; they represent examples of combinations of choices from 12 (originally 11<sup>171</sup>) different dimensions of the simulation universe. Each dimension has a variety of choices—a spectrum—to choose from ([Fig. 7.16](#)).



**Fig. 7.16 The 12 dimensions of simulation applications.** (A) Dimensions 1-9. \*These terms are used according to Miller's pyramid of learning.



**Fig. 7.16, cont'd. (B)** Dimensions 10-12. Any particular application can be represented as a point or range on each spectrum (shown by diamonds). This figure illustrates a specific application: multidisciplinary crisis resource management (CRM)-oriented decision making and teamwork training for adult intensive care unit (ICU) personnel. ED, Emergency department; M&M, morbidity and mortality; OB/GYN, obstetrics and gynecology; OR, operating room.

Any particular simulation activity can be classified by delineating one or more characteristics in each of the 12 dimensions. The different attributes can be combined as needed to achieve the pursued objectives. Clearly, some combinations are useless or irrelevant, some are similar to each other, and others are redundant, but the total number of unique combinations across all dimensions is still very large and only some combinations have been implemented. Dimensions of particular relevance are the goals and purposes of the simulation, the target population, the modalities of simulation, and the pedagogical approach that is used.

The content of many dimensions has been addressed in detail in the earlier parts of the chapter. Therefore, for the sake of completeness, only a short description of the dimensions is given here and the reader is referred back to each section for more information. Those who seek a detailed description of the different dimensions are referred to other literature where the model is described as a whole in detail.<sup>75,234</sup>

#### Dimension 1: Purpose and Aims of the Simulation Activity.

The most obvious applications of simulation have been described in the subchapter “Application of Simulators in Anesthesia and Health Care.” For more detailed information the reader is referred back to this section. To summarize the main purposes shortly, they are (1) education, (2) training including clinical rehearsal, (3) performance assessment, (4) research about simulation, and (5) research with simulation, including (5a) testing of procedures, (5b) testing of equipment, and (5c) system probing.

#### Dimension 2: Unit of Participation in the Simulation.

The units of participation have been described in the subchapter on the classification of simulation teams. For more detailed information the reader is referred back to this section.

#### Dimension 3: Experience Level of Simulation Participants.

Simulation can be applied along the entire continuum of education of clinical personnel and the public at large. For more information see earlier subchapter on the use of simulation in education and training. As mentioned earlier, simulation training is applicable to health care providers with a range of experience, including experts,<sup>2,50</sup> novices and advanced residents,<sup>2,90,178,235,236</sup> medical/nursing/other healthcare profession students,<sup>51,52,53-57</sup> and even children.<sup>58-61</sup>

#### Dimension 4: Healthcare Domain in Which Simulation is Applied.

Simulation techniques can be applied across nearly all health care domains.<sup>18</sup> A summary of the different domains was given in the earlier subchapter on “Use of simulation.”

#### Dimension 5: Healthcare Disciplines of Personnel Participating in the Simulation.

Simulation is applicable to a wide variety of professionals in health care, not only to physicians. In anesthesiology, simulation has been applied to novices and experienced trainees, board certified anesthesiologists, CRNAs, and anesthesia technicians. Simulation is not limited to clinical personnel. It may be directed at managers, executives, hospital trustees, regulators, and legislators.<sup>73,74</sup>

#### Dimension 6: Type of Knowledge, Skill, Attitudes, or Behavior Addressed in Simulation.

Different types of competences can be addressed with simulation: knowledge, skill, attitudes, behavior. Based on the Miller pyramid (see corresponding subchapter), competences can be classified with regard to their level of appearance to “knows,” “knows how,” “shows how,” and “does.” Apart from the competences described by Miller,<sup>197</sup> Gaba<sup>234</sup> added cognitive skills such as decision-making processes, attitudes, and behaviors to the competences that can be addressed with the spectrum.

### Dimension 7: Age of the Patient Being Simulated.

Simulation is applicable to nearly every type and age of patient. Fully interactive neonatal and pediatric patient simulators are available. Simulation can address aspects of end-of-life issues for every age.

### Dimension 8: Technology Applicable or Required For Simulations.

To accomplish the different simulation goals listed in dimensions 1, 3, 4, 5, 6, and 7 various simulation technologies—including no technology—are relevant for simulation. An overview is given in the earlier subchapters “History and Development of Simulators,” “Fidelity and Classification of Simulators,” and “So many simulators and simulation options: which one to use...?”.

### Dimension 9: Site of Simulation Participation.

The different sites of simulation have been described in detail in the correspondent subchapter. Video conferencing and advanced networking may allow even advanced types of simulation to be conducted remotely (see dimension 10).

### Dimension 10: Extent of Direct Participation in Simulation.

Not all learning requires direct participation. Some learning can occur merely by viewing a simulation involving others because the viewer can readily imagine being in the shoes of the participants.<sup>237</sup> A further step is to involve remote viewers with interaction in the simulation itself or verbal interaction in debriefings about what transpired. Several centers have been using videoconferencing to conduct simulation-based exercises, including morbidity and mortality conferences. Because the simulator can be paused, restarted, or otherwise controlled, the remote audience can readily obtain more information from the on-site participants, debate the proper course of action, and discuss with those in the simulator how best to proceed. Further steps of participation are personal involvement (“hands-on”) either in a replicated clinical site or immersive personal participation in an in situ simulation.

### Dimension 11: Feedback Method Accompanying Simulation.

One can learn a great deal just from simulation experiences themselves, without any additional feedback.<sup>238</sup> For many simulations, specific feedback is provided to maximize learning. On-screen-based simulators or VR systems, as well as the simulator (part-task trainer or mannequin) itself, may provide feedback about the participant’s actions or decisions, particularly for manual tasks for which clear metrics of performance are readily delineated. More commonly, human instructors provide feedback. This can be as simple as having the instructor review records of previous sessions that the learner has completed alone. For many target populations and applications, an instructor provides real-time guidance and real-time feedback to participants while the simulation is ongoing. The possibility to start, pause, and restart the simulation is valuable in this respect. Alternatively, brief post-hoc feedback is given by the instructor at the end of the simulation. For the most complex uses of simulation, especially when training experienced personnel, the typical form of feedback is provided by an instructor and is included in a detailed post-simulation debriefing session.<sup>105,107,112,113,238</sup> More discussion of debriefing is given later in the subchapter on “Debriefing.”

### Dimension 12: Embedding of Simulation in Relevant Organizational, Professional, and Societal Contexts.

The final important dimension is how the simulation

application is embedded into an overall context.<sup>159</sup> Being highly embedded may mean that the simulation is a formal requirement of the institution or is mandated by the governmental regulator. Another aspect of embedding may be that—for early learners—the initial (steep) part of the learning curve is required to occur in a simulation training before the learners are allowed to work on real patients under supervision. In addition, complete embedding of simulation into the workplace means that simulation training is a normal part of the work schedule, rather than being an add-on activity attended in the spare time of clinicians.

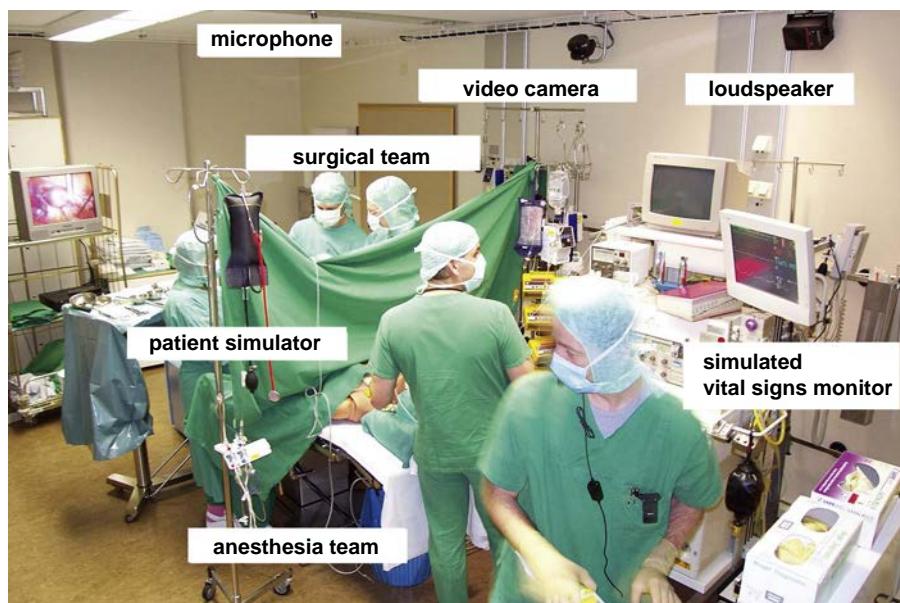
## Crisis Resource Management (ACRM; CRM): Part of Modern Patient Simulation Team Training

In the last subchapters, the benefits and the effectiveness of simulation-based education were highlighted and its ecologic validity was considered. This subsequent section now explores the idea that simulation-based education for a variety of simulation curricula, especially for team training, needs to take into account not only medical and technical skills, but also what is called anesthesia crisis resource management (ACRM), also referred to as crisis resource management (CRM). For detailed information on CRM see [Chapter 6](#).

### THE ROOTS OF ANESTHESIA CRISIS RESOURCE MANAGEMENT TRAINING

In 1989, based on earlier work, Cooper,<sup>239,240</sup> Howard et al.,<sup>181</sup> and Gaba<sup>241,242</sup> of the VA-Stanford and their colleagues identified gaps in the training of anesthesiologists regarding several critical aspects of decision making and crisis management that were not systematically taught during standard residency or postgraduate education. These gaps were inadequate learning and skills of (1) precompiled plans for dealing with perioperative events; (2) metacognition and allocation of attention; and (3) resource management behavior, including leadership, communication, workload management, monitoring, and cross-checking of all available information.

Historically, it had been assumed that anesthesiologists would acquire these plans and non-technical skills (see [Chapter 6](#)) by osmosis, solely by experience and by observing role models who had these qualities, rather than specific education and training about them. But similar to aviation, medicine had to learn that those kind of (non-technical) skills were not acquired unless specifically taught. For flight crews, CRM training was originally created to address these issues. Especially for anesthesia, but for other health care domains as well, the VA-Stanford group modeled their training after aviation CRM and named it ACRM.<sup>181</sup> For a broader use in health care, oftentimes ACRM is also referred to solely as CRM. The ACRM approach has been highly influential. ACRM curricula and ACRM-like curricula are taught at simulation centers around the world, not only in anesthesia, but in many other domains of health care, including ICU, emergency medicine, labor and delivery, trauma, and field responders.<sup>3,93,222,243-247</sup> [Fig. 7.17](#) shows a typical CRM crew training scenario.



**Fig. 7.17 Crisis resource management training scenario during crew training.** The surgical team is performing a complicated endoscopic surgical procedure replayed on screen. The anesthesia team must solve a clinical problem and coordinate with the surgical team. Video cameras, microphones, and loudspeakers provide the necessary connectivity and later debriefing tools. (Photograph taken by M. Rall at the Center for Patient Safety and Simulation, University Hospital, Tübingen, Germany.)

## ANESTHESIA CRISIS RESOURCE MANAGEMENT CURRICULA

A working group of the original ACRM centers (VA-Stanford, Boston CMS, Toronto Sunnybrook) promulgated a set of criteria to be met by a curriculum to be called either ACRM or ACRM-like. **Box 7.3** presents an excerpt of the criteria.

Among others, these criteria delineate:

1. To target the above mentioned identified gaps in training, approximately 50% of the emphasis of ACRM is on the medical and technical management of specific high-risk perioperative situations, and about 50% is on generic principles of crisis management that apply to nearly every complex patient care situation. The key teaching points of ACRM are shown in **Box 7.4**. These points are emphasized during the ACRM simulation course, and their occurrence or omission is highlighted during the debriefing sessions.
2. Special training is needed for instructors in ACRM-like curricula. The authors' experience suggests that the most difficult aspect of ACRM instructing is debriefing, and new instructors require a significant period of experience, preferably under supervision by more senior instructors, before being ready to be fully independent instructors. Several groups working separately or collectively have developed comprehensive training programs on simulation instruction, including substantial modules on debriefing and scenario design (see later subchapter on instructor qualification).
3. ACRM-like curricula employ a variety of teaching modalities to achieve these goals, including the following:
  - Comprehensive textbook on anesthesia crisis management: *Crisis Management in Anesthesiology* (now in an expanded second edition).<sup>24</sup> This book includes didac-

tic material on ACRM principles and a comprehensive catalog of critical incidents in anesthesia that provides guidelines for preventing, recognizing, and managing 99 perioperative situations in a uniform format. The catalog section of the text is intended to provide study material to increase anesthesiologists' stock of pre-compiled response plans to common and uncommon situations. This textbook has been translated into Japanese, German (first edition), Spanish, and Portuguese (second edition).

- Brief presentation and discussion reviewing the principles of CRM and patient safety.
- Use of trigger videos meant to initiate discussion, sometimes from a non-health care setting (e.g., commercial aviation, British warship during the Napoleonic wars).
- Group exercises analyzing a patient care event, presented as: (i) an actual patient care event captured on video or a reconstruction thereof; (ii) a video of a presentation as if from a morbidity and mortality conference; or (iii) a written report of the event.
- The core of simulation activities in ACRM-like curricula will be several hours of different, complex, multifaceted, realistic simulation scenarios in which participants rotate through different roles, including for example primary anesthesiologist, first responder (called cold, with no knowledge of the situation), and scrub tech. Other instructors or actors play the roles of surgeons, nurses, and technicians as in a real perioperative setting. Each situation is followed by a detailed debriefing (see later in discussion on "Debriefing").

Several publications have detailed the response of participants with varying levels of experience to ACRM training or its equivalent.<sup>181,248-250</sup> Participants have

### BOX 7.3 Characteristics of Anesthesia Crisis Resource Management-like Simulation Training

#### Objectives

- Learn generic principles of complex problem solving, decision making, resource management, and teamwork behavior.
- Improve participants' medical and technical, cognitive, and social skills in the recognition and treatment of realistic, complex medical situations.
- Enhance capacity for reflection, self-discovery, and teamwork and for building a personalized tool kit of attitudes, behaviors, and skills.

#### Aim

- Prevent, ameliorate, and resolve critical incidents.

#### Course Characteristics

- A realistic simulation environment replicates a relevant work setting (or an actual patient care setting with *in situ* simulation).
- Personnel will represent those persons found in the typical work environment of the participant, including nurses, surgeons, and technicians.
- The bulk of the training course consists of realistic simulations followed by detailed debriefings.
- Primary participants can request and receive help from other participants.
- Participants may rotate among various roles during different scenarios to gain fresh perspectives.
- Simulation scenarios may be supplemented by additional modalities, including activities such as assigned readings, didactic presentations, analysis of videotapes, role playing, or group discussions.
- Training involves significant time (>4 h, typically ≥8 h) and is conducted with a small group of participants.

#### Content Characteristics

- Scenarios require participants to engage in appropriate professional interactions.
- At least 50% of the emphasis of the course is on crisis resource management behavior (nontechnical skills) rather than medical or technical issues (non-technical skills are discussed in Chapter 6).
- Observation only is not equivalent to actual participation in one or more scenarios.

#### Faculty Characteristics

- Training is intense and entails a high level of involvement of faculty with the participants and a low participant-to-faculty ratio.
- Faculty members, especially those leading debriefing, have special training or experience in conducting crisis resource management-oriented training.

#### Debriefing Characteristics

- Debriefings are performed with the whole group of participants together and use (as appropriate) audio-video recordings of the simulation sessions.
- Debriefings emphasize constructive critique and analysis in which the participants are given the greatest opportunity possible to speak and to critique and to learn from each other.

been extremely positive about their experience in the ACRM course, and most believe that it contributes to their safe practice of anesthesia.<sup>180</sup> In training settings

### BOX 7.4 Key Points in Anesthesia Crisis Resource Management

A detailed explanation of the crisis resource management key points is given in *Chapter 6*. The key points are derived from the publication of Rall and Gaba in the sixth edition of Miller's Anesthesia<sup>367</sup> and presented here in their updated, current version.

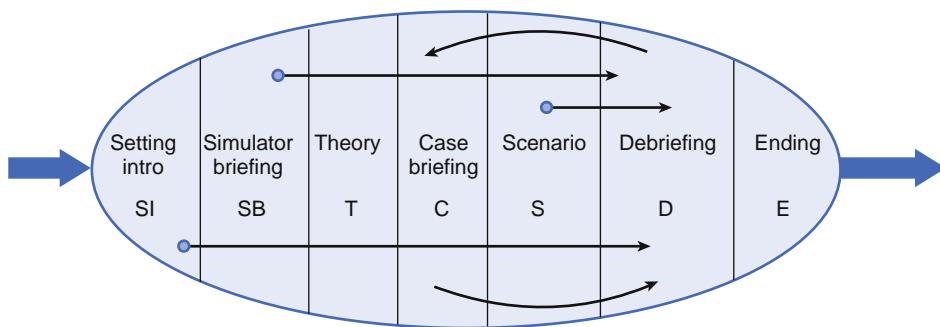
1. Know the environment.
2. Anticipate and plan.
3. Call for help early.
4. Establish leadership and followership with appropriate assertiveness.
5. Distribute the workload. Use 10 s for 10 min concept.
6. Mobilize all available resources.
7. Communicate effectively—speak up.
8. Use all available information.
9. Prevent and manage fixation errors.
10. Cross and double check. Never assume anything.
11. Use cognitive aids.
12. Reevaluate repeatedly. Apply 10 s for 10 min concept.
13. Use good teamwork. Coordinate with and support others.
14. Allocate attention wisely.
15. Set priorities dynamically.

where “practice improvement” is a specific target such courses can trigger credible efforts at personal or system change.<sup>248</sup> At the Stanford residency, ACRM has been extended to a multilevel course conducted over several years (i.e., ACRM 1, 2, 3). As the course levels progress, the scenarios become more complex and involve subspecialties of anesthesia. Besides, additional teaching modules cover other important aspects of organizational safety, such as systems thinking in morbidity and mortality conference settings or peer review settings, follow-up response to severe adverse perioperative events, and disclosure to the patient or family of bad news after an adverse event.

ACRM courses and ACRM-like variants are now offered worldwide and are often mandatory for trainees (and in some cases for experienced personnel). Salas and colleagues published an excellent critical overview about prerequisites for effective CRM training.<sup>251</sup>

### BENEFITS OF CRISIS RESOURCE MANAGEMENT-BASED SIMULATION TRAINING

The literature on published benefits of CRM training effects is large; here are a few examples. Knudson and colleagues found a significant improvement in overall and teamwork scores in surgical residents taking care of critically injured simulated trauma patients if the residents had undergone CRM-like simulation training.<sup>90</sup> In a simulation study, no-flow time rates were significantly lower after CRM training paralleled with improved leadership verbalization.<sup>153</sup> A study in a multidisciplinary obstetrical setting involving anesthesia professionals showed a significant improvement in interprofessional teamwork and improved stress recognition after a CRM intervention.<sup>220</sup> In a prospective 3-year cohort study Haerkens and colleagues showed a decline in serious complications and the standardized mortality ratio, decreasing occurrence of cardiac arrests, and improving cardiopulmonary resuscitation success rates



**Fig. 7.18 Anatomy of the simulation exercise.** A simulation exercise consists of different modules or different phases (e.g., simulation introduction [SI], simulator and clinical environment briefing/“familiarization” [SB], theory input [T], case briefing [C], scenario [S], debriefing [D], ending [E]). This figure shows a typical flow for a simulation course. If more than one scenario takes place during the course, the sequence from [C] to [D] is repeated for each scenario. The different modules are interrelated, and problems arising in one module can affect other modules (thin arrows). (Figure with courtesy of P. Dieckmann.)

after a CRM-based intervention in a 32-bed ICU.<sup>252</sup> Moffatt-Bruce et al. published a significant reduction rate of adverse events and described return on investment after a system-wide implementation of CRM in 12 different hospital units including perioperative staff.<sup>253</sup>

## Anatomy of a Patient Simulation Team Training Exercise

Whenever simulation is used it is important to consider its conceptual basis and the contextual factors that influence its use.<sup>254,255</sup> Therefore, with a focus on (CRM-oriented) mannequin-based patient simulation conducted for health care professionals, the next subchapters (1) give an overview of the training setting and important elements of a simulation exercise; discuss (2) the design of simulation scenarios and their execution; and (3) the modalities of the professionals’ debriefing after a simulation scenario. Even though focused on the mannequin-based patient simulation conducted for health care professionals, many of the conceptual approaches presented below are identical or need to be modified only slightly to encompass other choices in the 12 dimensions of simulation.

Simulation activities vary in terms of goals and objectives. Most of the time, simulation scenarios are integrated into a multifaceted curriculum, which itself must be situated relative to the overall educational and training pathway of individuals and groups. Hence, for any given simulation activity both the conceptual and physical setting influence how the exercise is conducted, how it is perceived by participants, what participants learn, and which learned items are applicable in the clinical work domain.<sup>255</sup>

A simulation course/training itself can be divided analytically in different, interconnected phases as shown in Fig. 7.18.<sup>255</sup> Not all phases need to be present at each exercise and conversely some phases—like “scenario” and “debriefing”—may be repeated several times in a longer session.

Optimally the interconnected phases of the simulation exercise should be coordinated. If, for example, the briefing/familiarization is inadequate, participants may not be able to properly immerse themselves in the scenarios and debriefing might be impaired. The role of the simulation instructor changes throughout the different phases of the simulation training—from providing instruction in the

beginning of a course to facilitating learning during debriefing. Based to a large extent on the work of Dieckmann,<sup>255</sup> the different phases of a simulation exercise (see Fig. 7.18) are discussed next, using the timeframe and elements of a simulation-based course as an example.

**Pre-Briefing (PB).** The pre-briefing introduces or reminds participants in advance about the course, its goals, and processes to appropriately situate the activity in their overall training, establish a positive attitude, and review the schedule of activities. An exercise that can be useful (stemming from advice from Ruokamo and Keskitalo from the University of Lapland) is to ask and discuss with participants “what do you want to learn or explore” in today’s simulation course?, and similarly to ask the instructors “what are you interested in teaching or exploring?” This conversation engages the participants and demonstrates the instructors’ interest in trying to address many of the preferences of the learners.

**Simulation introduction (SI).** An important aspect at the beginning of a session is to provide an overview about the course and the rules and norms of conduct for the set of exercises.<sup>256</sup> It is also important to provide a shared understanding for the simulation participants of the events that transpire during the course.<sup>111</sup> Besides, it is important to create a positive atmosphere to maximize learning, often referred to as “psychological safety,” or as recently published a “safe container.”<sup>121</sup> Edmondson has defined psychological safety as “*the shared belief that the team is safe for interpersonal risk taking.*”<sup>257</sup> Often this has a lot to do with ensuring the confidentiality of the simulation environment (i.e., “what happens here stays here”) and that debriefings will “critique the performance, not the performer.” Psychological safety “*is not about creating a comfortable space, it is about making it ‘ok’ to be uncomfortable.*”<sup>258</sup>

**Simulator and clinical environment briefing (SB) (“familiarization”).** Participants need to be familiar with the simulator and the simulated environment in order to perform the closest to reality as possible, and they should not be distracted by technical or procedural uncertainty during the scenario. The participants can best master the scenario and actively engage in it if they know (1) how the simulator works (“normal” breathing sounds, “normal” pulses, intubation, intravenous access, etc.); (2) what it is able to do or not do; (3) how the

simulated environment works (how to call for help, how to use the simulated equipment, etc.); and (4) what participants are able to perform on the simulator and what they need to pretend doing. Familiarization is characterized through explanations, demonstrations, and hands-on time for the participants themselves. This phase is very important in order to help the participants to make the best use of the simulation experience during the scenario. The plastic mannequin is on the way to being seen and treated as a patient. The more comfortable participants feel with the simulator and the simulation equipment, the less they will be scared or tense during the scenario. And more reflective learning about medical and non-technical skills can take place during the debriefing because the debriefing will not become about discussing the confusions and challenges regarding the simulation technology or environment. Therefore, it benefits both the instructor and the participants to have enough time for the familiarization process.

**Presentation or discussion of theory (T).** Theories of human performance or of clinical work processes might or might not be part of the course. Most exercises have didactic or theory components on relevant content information. Those components can either serve for transfer of (new) medical or technical knowledge, or for a refresher lecture on certain algorithms, but also for the introduction of (anesthesia) crisis resource management-related skills (ACRM, CRM) and patient safety issues (Chapter 6). Sometimes educational material is made available in advance through readings or online exercises. Sometimes lectures or group-work modules are put in place at different junctures of the training.

**Breaks (B).** For complex and long-lasting courses breaks are important for recreation and for socialization among participants and with instructors. Breaks provide a venue for informal sharing and storytelling, one of the many learning opportunities during a simulation training outside of a simulation scenario.

**Case briefing (C).** Because the simulator is not a real patient itself providing clinical information and because the environment of a simulation imposes several challenges, there are different ways to ensure that participants have certain relevant information concerning the case and the simulation reality before, or at the beginning of, the scenario. Sometimes it is natural for a participant to take over a case from another clinician (in fact in ACRM starting every case from the beginning would waste a lot of time). Such a handoff can be scripted to be complete or cursory as appropriate. In other cases the context information can be presented verbally or in written form by an instructor. Other information that would not be readily available in context might include the look or smell of the patient or the specific location of care (e.g., main OR vs. off-site ambulatory surgery center).

**Simulation scenario (S).** The scenario and—when possible—the debriefing together form the core of the learning experience during simulation. Simulation scenarios are more than clinical cases. They are the vehicle to reflect on medical knowledge as well as personal and team performance in a safe learning environment that elucidates similar behaviors as during real-world cases. Most simulation exercises involve a scenario that simulates a given clinical

situation, challenging the participants to deal with the situation at hand. The scenario is designed in advance by the instructors in accordance with the learning objectives of the training (see later subchapter on scenario design). During the execution of the scenario, the instructor (or simulationist/simulation technician) regulates the responses of the simulator and adapts the scenario flow<sup>259,260</sup>; gives relevant patient, situation, or clinical information to the team that the simulator or clinical personnel does not provide itself<sup>260,261</sup> (see later subchapter on live in-scenario guiding); manages the exercise to enable participants to optimally act as if<sup>259</sup> treating a real patient (see later subchapter on scenario design).

**Debriefing (D).** Most training scenarios are immediately followed by some form of feedback or debriefing, respectively. Fanning and Gaba give an overview of the origin and background, the role, the models, the structural process, the elements, and several other modalities of debriefing in simulation-based learning in their recommended review.<sup>238</sup> The learning objectives, the target audience, and the simulation modalities drive the decision whether a debriefing is useful and if so how in-depth the debriefing process needs to be. In some courses, feedback is only minimal, whereas other courses have a dedicated debriefing session after each scenario that take as long, or even longer, than the scenario itself (see later subchapter on debriefing techniques). Several different debriefing methods exist.<sup>24,105,109,110,238</sup> Debriefing can be facilitated sometimes by strategically presenting snippets of the recording of the scenario.<sup>117,238</sup>

**Ending (E).** Especially for multiple-scenario courses, a separate final session may be included to end the course. This phase represents an opportunity to summarize issues that were covered and to reflect on how best to apply these lessons to real patient care.

## Scenario Design and Execution: Knowing the Learning Objectives and Making It Real

The design of scenarios for interactive simulation team trainings can be tricky and typically differs from preparing training exercises for traditional curricula.

“The key is the program, not the hardware”<sup>62</sup> was a truth about simulation learned early in aviation simulation and similarly possesses validity for the scenario design and execution with patient simulation. Using simulation in a goal-oriented way is at least as much about the conceptual aspects of the technique as it is about the technology of the simulation devices. An understanding of the conceptual and theoretical aspects of simulation is helpful for determining the right applications of the technique and the important matchups to be made in the design and conduct of simulation exercises to obtain the best results. When used most effectively, simulation can be—to borrow a line from the music band U2—“...even better than the real thing.”

In the following sections the design and conduct of scenarios for a patient simulation are touched on more closely, considering (1) establishing learning objectives; (2) applying cognitive load theory to scenario design; (3) pointing out constraints and limitations of the design, discussing

(4) conceptual issues of reality, realism, and relevance; and (5) in-scenario information and guiding.

There is a vast aggregation of literature concerning instructional design for all kinds of simulation applications. For detailed information the reader is referred to further literature.<sup>23,77,115,177,262</sup> The topic is covered extensively in most of the instructor training curricula that are offered at sites around the world. International and regional simulation meetings (e.g., the International Meeting on Simulation in Healthcare [IMSH] of the SSH, or the annual meeting of the Society in Europe for Simulation Applied to Medicine [SESAM]) often provide workshops on scenario design. The user groups of the major simulator manufacturers also have workshops on the topic.

The following sections can only serve as an introduction to the topic and again focus mainly on (CRM) mannequin-based patient simulation conducted for health care professionals.

## GOAL ORIENTED: ESTABLISHING LEARNING OBJECTIVES

Learning objectives provide the reason and frame for the simulation scenario. They contain clinical and technical skills, or non-technical skills such as communication, leadership, teamwork, situation awareness, decision making, and task management (see Crisis Resource Management, CRM, [Chapter 6](#)). Optimally, scenarios are chosen that stress the individual's diagnostic and problem-solving abilities, the clinical and technical knowledge, and the core aspects of CRM.<sup>75,217</sup>

Learning objectives can be preset by a curriculum, determined via needs analysis, intuitively known by the simulation-savvy clinician educators, or learned about in instructor training or in the literature. Learning objectives operationalize relevant questions by defining who should be able to do what and in what situations.<sup>78</sup>

Simulation scenario design may be thought of in a step-wise, layered fashion. Research in work psychology suggests that, for the purpose of learning, it is helpful to de-construct complex tasks into phases and hierarchical levels. For example, the scenario "resuscitate the patient" includes three main goals: (1) diagnose cardiac arrest (subgoals: check pulse, check breathing, check "brain"), (2) oxygenate brain (subgoals: open airway, cardiac massage, ventilate), and (3) reestablish spontaneous circulation (subgoals: defibrillate, administer epinephrine) which require team members to coordinate (e.g., ensure that all team members know diagnosis, distribute task).<sup>263</sup> This insight into what behaviors are expected of a team during the scenario facilitates not only the design of the scenario as such,<sup>115</sup> but it also helps educators to direct their attention while observing the team's performance and possibly sharing the workload among them by distributing observational tasks in the co-debriefing setting.<sup>264</sup> Furthermore, it helps educators to guide the debriefing.<sup>107</sup> Learning objectives and performance expectations should be considered in advance in order to use the debriefing to close potential gaps and guide teams to maintain good performance.

## COGNITIVE LOAD THEORY: NOT TOO MUCH, NOT TOO LITTLE

When designing and conducting simulations the learning opportunity would ideally match the abilities and learning

needs of the participants. If the scenario is too difficult, participants' can be overwhelmed and their learning likely compromised. Conversely, if the scenario is too easy, participants will find no challenge, may be bored, and won't learn very much. Cognitive load theory<sup>265</sup> provides a framework to distinguish different aspects in a learning situation that illuminate the "difficulty" of a scenario so as to optimize it for learners. In this theory, three different forms of cognitive load are distinguished. The overall difficulty can be thought of as the sum of the following three parts: (1) Intrinsic cognitive load, which describes the complexity/difficulty of the material to be addressed. This depends somewhat on the learner's prior knowledge but beyond that some issues are just more complex than others for most. (2) Extraneous load, which stems from the presentation of the material to be learned, e.g., a well-structured textbook might make learning easier compared to a chaotic lecture. (3) Germane load, which describes the internal processes and the cognitive energy needed to process information.

Cognitive load theory would suggest, for example, that asking novice anesthesia professionals to manage both a complex clinical situation and a challenging interpersonal one may result in overload. Unfamiliarity with simulation will also raise the extrinsic load—participants have to interpret the pretend situation as if it is the real thing, making it difficult to concentrate on the lessons to be learned. The germane load might be increased when participants are concerned about being observed. They not only need to consider what the best course of action in the scenario might be, but, at the same time, also try to manage the impression that they make on the instructors and observers.

A good simulation scenario will take these different elements into account. Extraneous load can be optimized by carefully designing scenarios and by PB instructions.<sup>255</sup> Germane load might be optimized by helping participants become more familiar and comfortable being in simulations, for example, by well-designed simulation familiarization, or by increasing the complexity of scenarios slowly.

## CONSTRAINTS AND LIMITATIONS OF SCENARIO DESIGN IDEAS

It is easy to suggest a scenario on paper but more difficult to translate it into an effective scenario for actual use. Limitations and constraints of the available simulators, personnel resources at hand, the props or external systems that would be needed, and the time needed to set up and run the proposed scenario must be considered. Most scenarios are first generated with a core idea, a "kernel" that is then fleshed out by discussion in an iterative fashion, with creative redesign or minor technical modifications. Ideally the new, redefined scenario is tested out first by instructors and technical staff, or pilot-tested with a volunteer group of participants from the target population. With highly experienced instructors a new scenario may need only a technical walkthrough before it is run for real participants. All scenarios can get better with time as glitches are found and refinements made.

## SCENARIO DESIGN TEMPLATES AND SCENARIO TEMPLATES

Many centers have developed design templates for the development of their scenarios. [Box 7.5](#) shows the key questions

## BOX 7.5 Key Considerations for Simulation Scenario Scripts

Based on script templates provided by Dieckmann and Rall (<https://www.inpass.de/downloadshtml/downloadscenarioscript/>), the key information a scenario script should provide includes:

- Scenario name (quick reference)
- Major medical challenge of scenario
- Major cockpit resource management (CRM) challenge of scenario
- Learning goals (medical and [!] CRM)
- Brief narrative description of scenario
- Staffing (instructor/simulation team and participants)
- Case briefing (all participants together or separate briefings for different teams)
- Simulator setup and mannequin preparation
- Props needed
- Scenario “lifesavers”<sup>259</sup> for both excellent and bad performance of participants

Usually, the scenario script contains (1) a summary sheet with brief notes of the above mentioned topics and (2) a more detailed description of the scenario in regard to those questions on several other pages. The proper use of scenario scripts is a regular part of many instructor training courses.

for the design of scenarios. Long scenario templates that are freely available include Dieckmann and Rall's (<https://www.inpass.de/downloadshtml/downloadscenarioscript/>) and the Duke University template ([https://anesthesiology.duke.edu/?page\\_id=825706](https://anesthesiology.duke.edu/?page_id=825706)). Some journals publish detailed scenario descriptions and some professional societies have created scenario repositories for members; the American Society of Anesthesiologists (ASA) Simulation Committee has a repository for scenarios to be shared among its ASA-endorsed simulation programs. By now, many scenario templates are freely available on the Internet. In general, long and detailed templates are only needed when a scenario is to be shared widely, or when there is a need to formally document it. Simpler templates will likely suffice for in-house use by a single simulation center.

## REALITY VERSUS REALISM

Simulation is a complex social undertaking.<sup>155</sup> The concepts discussed in the upcoming section concern the nature and the impact of “fidelity” and “realism” as they apply to simulation and the goals of simulation. Both are terms widely used, and misused, in simulation design. In this chapter the concept of relevance is covered briefly. All three concepts are important components of engaging participants during simulation, an important aspect of conducting meaningful exercises.

A patient simulation exercise is itself a real occurrence that is actually happening. The exercise is a *reality*, but it is intended to represent another reality in the real world of patient care. Hence, it may or may not be perceived that way. “Realism” addresses the question of how closely a replication of a situation is needed to meaningfully represent this situation to participants. Aviation simulators, for example, are so realistic now that pilots with experience flying one aircraft are routinely certified to fly a totally new or

different aircraft, even though they have never flown the actual aircraft before. Nestel, Krogh, and Kolbe explored realism in health care simulations in detail.<sup>266</sup> In their work, the authors also use the term “*meaningfulness*” in proposing strategies to help simulation educators make sense of decisions about realism.

There is an important distinction between the realism of a *simulator* (a device) and that of a *simulation* (the exercise). For example, a simulator could be indistinguishable from a real human being (e.g., an actor playing a standardized patient) and yet be used in an implausible and useless fashion, so that the simulation itself is not realistic. Conversely, certain kinds of simulation realism can be evoked by exercises that use simple simulators or even no simulator at all (see below).

It is naïve (though frequent) to think that greater realism of a simulation exercise will automatically lead to better achievement of its goals. Maximum “realism” is neither needed nor desired for every type of simulation endeavor. For some applications with some target populations, it can be highly advantageous to reduce the realism to heighten the learning experience.<sup>157</sup> On the other hand, merely creating a realistic simulation does not guarantee meaning or utility (e.g., learning) for the participants.<sup>155,156</sup> The different concepts and explanations with regard to this matter have been discussed repeatedly in the literature.<sup>155-158,260,267-269</sup> However, as “realism” is a complicated set of ideas in simulation, results of studies trying to investigate roots and effects of simulation realism are not conclusive, in part because each study may concentrate on a different aspect of the complex whole. Different fidelities and dimensions are used to describe or achieve the realism of simulation, as described in the following.

### Different (practical) fidelities to create simulation realism.

Alessi<sup>270</sup> defined fidelity as the “degree to which a simulation replicates reality” (p. 203). Several concepts about simulation fidelity exist.<sup>198,260,271</sup> These include physical fidelity (the device replicates physical aspects of the human body), environmental fidelity (the simulation room looks like the relevant clinical site), equipment fidelity (the clinical equipment works like or is the real thing), and psychological fidelity (the simulation evokes behaviors similar to the real situation). Realism is thought to be achieved by various forms of validity, such as face validity (looks and feels real to participants), content validity (the exercise covers content relevant to the target situation), construct validity (the simulation can replicate performance or behavior according to predefined constructs about work in real situations), and predictive validity (performance during a simulation exercise predicts performance in an analogous real situation).

### Different (theoretical) dimensions to create simulation realism.

In 2007, Dieckmann, Gaba, and Rall published an article attempting to clarify some issues about realism, reality, relevance, and how they influence the purpose of conducting simulations.<sup>155</sup> In their article, they applied the model of thinking about reality by the German psychologist Laucken to the realism and fidelity of simulation. Laucken described three modes of thinking about reality: physical, semantic, and phenomenal fidelity. Another publication on modes of thinking about

reality was published by colleagues from Boston.<sup>158</sup> Apart from those definitions a variety of terms exist to describe conceptual simulation design, in particular with regard to fidelity. To gain a better understanding of the various terms and their meaning, Paige and Morin published a systematic review article on that matter and additionally suggested to divide the concepts of fidelity into physical (including environmental and equipment), conceptual, and psychological.<sup>260</sup> The ideas and concepts presented below are largely contributed by Dieckmann and his adaptation of broader psychological concepts to simulation in medicine:

*Physical mode of realism.* The physical mode concerns aspects of the simulation that can be measured in fundamental physical and chemical terms and dimensions (e.g., centimeters, grams, and seconds). For example, the weight of the mannequin, the force generated during chest compressions, and the duration of a scenario all are physical aspects of simulation reality. Despite their roughly human shape, existing mannequins have many unrealistic physical elements, for example they are made of plastic, not flesh and bone; they may have unusual mechanical noises detectable during auscultation of the chest; the “skin” does not change color.

The physical mode of simulation also relates to clinical equipment and the clinical environment. (1) Some equipment used in mannequin-based simulation is fully functional and physically identical to the real thing. Labeled syringes may contain only water instead of real medications. (2) An ISS in an actual hospital room and bed has a higher physical realism than does the same equipment in a conference room.

*Semantic mode of realism.* The semantic mode of realism concerns concepts and their relationships concerning clinical information and its meaning. For example, in a simulation of hemorrhagic shock, how does the participant make sense of what is going on? Within the semantic mode, a simulation of hemorrhage could be described in semantical terms as “bleeding” of flow rate  $x$  beginning at time  $y$  occurring at site  $z$  that is associated with a blood pressure of  $b$  that shows a decrease after some time from the prior value of  $a$ . It is semantically irrelevant how the information is transmitted or represented. The same pieces of *information* could be represented either using a vital signs monitor, a verbal description, or the tactile perception of decreasingly palpable pulses. The semantic mode allows the simulation exercise to represent a real situation. It allows lifeless, rosy, smiling simulators to be treated as if they were real patients. It allows water-filled syringes to be treated as if they contain effective drugs.

#### PATIENT SIMULATION ACTION BOX

If the right and sufficient clinical information is given to the participants at the right time, in their minds the inanimate mannequin can become a severely ill patient (see later section on “in-scenario information and guiding”). At the same time it is important for instructors to remember, in particular during the debriefing, that because meaningful simulation depends on interpreting information, it is not always interpreted by participants the way that the instructor imagines it will be.

*Phenomenal mode of realism.* The *phenomenal mode* deals with the learner’s engagement and experience in the simulation including emotions, values, motivation, self-awareness, and beliefs. If participants are fully engaged in the simulation, then they are likely to act as if they are treating a real patient in the real clinical environment. For many purposes, providing high phenomenal realism is the key goal, but sufficient physical and semantic realism are means to this end.

#### PATIENT SIMULATION ACTION BOX

A good simulation scenario does not necessarily need to be designed as realistic as possible, for example having artificial blood all over the mannequin during a trauma scenario. A good simulation scenario can create the appropriate sense of realism by a combination of the following:

- (1) ... the simulator and environment used
- (2) ... the case presented, the team composition, and the professional role of each participant
- (3) ... clinical equipment used, or sufficient semantic equivalents
- (4) ... the briefing before the simulation case starts
- (5) ... instructor feedback when the simulator is examined (see later section, “live in-scenario information and guiding”). The application of those aspects is not trivial; they influence the way the simulation is perceived by clinical professionals.

#### SIMULATION REALISM AND SIMULATION RELEVANCE

The relevance of a simulation exercise concerns the match between the characteristics of the exercise and the reasons for which the exercise is conducted. Scenarios should be relevant to the trainees, but this depends on many factors, including the trainees’ backgrounds and experience, the method of conducting the scenario, and related parts of the simulation course (e.g., familiarization with simulator and simulated environment, case briefing, etc.).

In fact, it is worth utilizing unrealistic elements (“unreality”) in order to maximize the learning—a useful slogan is “the point is not to ‘fool’ them but rather to teach them.” So, for example, when training on invasive procedures, it is typical to forego phenomenal realism and emphasize physical and semantic realism so that psychomotor skills can be the focus. Similarly, physical realism may be sacrificed when necessary by time compression or expansion. Boring parts of a case may be skipped for experienced personnel whereas for inexperienced clinicians situations that could become lethal extremely quickly (e.g., swap of  $\text{N}_2\text{O}$  for  $\text{O}_2$  in the pipeline) may be slowed down so that inexperienced clinicians can try to think their way out of the problem. If such a situation were allowed to evolve at its normal speed, it would transition to management of cardiac arrest before the participants could deal with the original problem. Other uses of “unreality” include cognitive scaffolding, which provides various forms of assistance—sometimes a teacher or coach in the simulation room—or extra cues to help participants as they struggle with decision making and therapy selection.

## IN-SCENARIO INFORMATION AND GUIDING

Although full-scale mannequins mimic a wide range of human features, they differ from the body of an actual patient. This gap implies a need for simulation instructors to provide in-scenario information to help participants understand scenarios. In-scenario information and guiding may also be needed to help (early) learners progress in the scenario if they are stuck or on the wrong path. Different terms such as clues, triggers, prompts, hints, and instructional support have been found in the literature associated with the concept of cueing in a simulation activity.<sup>260</sup> Dieckmann et al. used the unique phrase “scenario life savers.”<sup>259</sup> Many cues and “life savers” can be used within the logic of the scenario in ways that do not disrupt the experience.

In general, one good way to feed information to participants in patient simulations about various phenomena that cannot be simulated physically is to announce the missing signs, symptoms, or examination results. Escher and colleagues summarized four methods that instructors used to provide such extra scenario information and how the different methods to convey information affected how scenarios played out.<sup>261</sup> The methods found included cues from (1) confederates, (2) bystanders, (3) loudspeakers from the control room to the scenario room, or via (4) an earpiece. Even though Escher et al. conclude that the mediation of information by a loudspeaker or an earpiece from the adjacent control room could be disturbing for team communication, the authors of this chapter see several advantages in the use of in-scenario audio guidance. In their opinion, audio guidance is especially helpful for feedback in those kind of situations: (a) physical examination results, such as (misleading) auscultation results, or results of abdominal palpation but usually only after the participant has credibly attempted to obtain that result physically; and (b) *immediate* correction of mental models that are not in line with the scenario (i.e., (misleading) auscultation apparently indicates pneumothorax, but there is in fact no pneumothorax).

This kind of in-scenario semantic information is incorporated by participants into their mental model of the situation at hand during the simulation and helps them to “stay in” the simulation despite physically treating a plastic mannequin.

## Debriefing: Heart and Soul of Patient Simulation

As introduced in the section on the “anatomy of a simulation course” (see Fig. 7.18), conducting simulation training is not only about running the simulation scenario but equally about how, in debriefing, the participants are facilitated to reflect about what they experienced. The philosophy of teaching and learning in a debriefing of a CRM-based simulation course differs from the traditional clinical teaching style (Table 7.3).<sup>238</sup> For more information on debriefing in health care simulation the reader is referred to further literature.<sup>24,105,109-111,113,238,272-276</sup> This chapter can only serve as an introduction to the topic and focuses mainly on patient simulation with focus on (CRM) team training.

**TABLE 7.3** Traditional Teaching Versus Facilitation in Simulation Training Courses

Traditional Teaching: “Teacher”	New way of teaching: “Facilitator”
Focus on theoretical or clinical knowledge only	Focus additionally on human factors/CRM
Focus on “what” happened/“what” or “who” was wrong	Focus on “why” things went wrong (deeper analysis) and on “why” things went well
(T) is the (absolute, infallible) expert.	(I) possesses expertise, but moderates different ideas on eye level, uses knowledge and expertise of (P), discusses own views with peers.
(T) tells participants what to do better next time.	(I) helps (P) to find out root causes for their performance, examines possible solutions together.
(T) knows what is right / important for (P).	(I) helps to self-reflect, gain realistic self-awareness / consciousness; (I) guides debriefing toward interesting areas, but is open for topics relevant to (P).
(T) speaks the most during feedback.	(I) stimulates and guides discussion among participants during debriefing, but does not speak the most.
(T) is a domain expert.	(I) additionally is a CRM expert.
(T) has no special training in patient simulation-based learning.	(I) has special training and/or experience in patient simulation-based learning.
(T) makes no video-assisted feedback.	(I) makes strategic use of video when relevant to enhance debriefing.
(T) determines whether (P) has learned the intended lesson.	(I) gauges whether (P) is engaged in discussion and understands relevant issues but (P)’s experience is too complex to assess simply

CRM, Crisis Resource Management; (I), Instructor/Facilitator; (P), Participant; (T), teacher.

## SIMULATORS (DEVICES) DON’T TEACH

Most simulation training exercises involve some kind of feedback or debriefing that can be given in many different ways and settings.<sup>111,113,238,272-275</sup> The terms *debriefing* and *feedback* are often used synonymously, but there exists a difference in their meaning. *Feedback* is used with the intention to modify thinking and / or behavior and generally involves comparing the observed performance to a standard (whether formally or informally defined). Usually it is a one-directional flow of information about the performance from the instructor to simulation participants.<sup>111</sup> *Debriefing* refers to a special time and format for discussing an episode of action in the past; it is the counterpoint to a briefing, which occurs before an action or task. In contrast to feedback, debriefing is viewed as a bidirectional, interactive, and reflective discussion or conversation that “may occur between simulation participants and facilitators [instructors], or among participants themselves, or some combination thereof” [p. 209].<sup>111</sup>

In medicine, inspired by its use in aviation CRM, the debriefing concept was introduced to simulation training by Gaba and colleagues as part of ACRM simulation training for anesthesia teams.<sup>181,217</sup> Over the years debriefing

after simulation training has been refined so that it has become an indispensable component of many simulation curricula.<sup>273</sup>

## INSTRUCTION VERSUS FACILITATION—A NEW WAY OF TEACHING

In many learning contexts, the person who is in charge of the training usually is referred to as “instructor.” In the debriefing idea described above, the instructor’s role changes from an “instructor” to a “facilitator”: instead of constantly instructing, the instructor’s role is to *facilitate* the learning process. This is accomplished by *directing the participants* to the most interesting and important areas for consideration, *stimulating discussion* among participants to *find underlying issues* for their performance and *seeking individual solutions for future events* of similar type. For most instructors, *facilitation* is a new way of teaching and often must be learned, even if they have many years of traditional instructor teaching experience. In the simulation arena the term instructor refers to an individual who is responsible for overall direction of a simulation scenario; that person is often—but not always—one of the facilitators for the debriefing.

Fruitful discussion and learning can be triggered by reflecting on both aspects of performance that worked well and those that were difficult or problematic (see also “Safety II”, chapter 6). In their paper Dieckmann et al.<sup>277</sup> describe the “learning from success” approach to simulation and debriefing drawing on several theoretical frameworks.

### PATIENT SIMULATION ACTION BOX

Ideally, the clinical expertise of the simulation participants should be represented in the clinical expertise of the instructors. For an interprofessional trauma team training, for example, it would be best to have instructor(s)/debriefer(s) from each of the relevant professions and disciplines, especially from anesthesiology, nursing, and surgery.

## DEBRIEFING TECHNIQUES

Although debriefing styles differ at institutions, sites, and individuals around the world, a common ground is shared by most simulation-based educators: debriefing should *stimulate self-reflection*, and it should unpack *how* and *why* things happened the way they did.

Reviews of debriefing techniques in simulation by Fanning and Gaba,<sup>238</sup> Cheng et al.,<sup>113</sup> and Sawyer et al.<sup>111</sup> indicate the broad range of literature available regarding debriefing, and highlight the many models and approaches that can be used. Debriefing most commonly occurs soon after a scenario run, but the same techniques can be used during pauses in the simulation. Although it is possible for participants to debrief themselves, this would come with limitations due to lack of structure. Usually a post-event debriefing is guided by a facilitator.<sup>111</sup>

A variety of approaches to debriefing exist, each with its own structural phases and several conversational structures.<sup>238</sup> These include Debriefing with Good

Judgement,<sup>105-107</sup> The Diamond,<sup>108</sup> SHARP,<sup>278</sup> PEARLS,<sup>109</sup> TeamGAINS,<sup>110</sup> Alternatives and Pros & Cons,<sup>238</sup> and others.<sup>111-114</sup> These conversational structures guide the flow and the context of the debriefing and divide it into various phases, each serving a specific focus and purpose. Whereas the phases differ, Sawyer and colleagues summarize that most frameworks highlight the importance of guiding the conversation from a beginning, through an examination of events, and then relate the aspects most relevant for clinical practice.<sup>111</sup> An example of a debriefing structure is shown in Table 7.4.

Although it is clear that debriefing plays a crucial role in simulation exercises,<sup>119,198,279-281</sup> there is little evidence supporting one format over another. This should not be surprising because the goal is broad, the experience of simulation is intense, and participants’ interpretations and discussion are rich.

A qualitative interview study<sup>275</sup> with 24 expert debriefers showed that for experienced debriefers it is not about the specific concept, but about the sets of ideas and beliefs that represent the values and teaching philosophy used: “*the debriefer is a facilitator, who must be dedicated, honest, genuinely curious and possess the abilities to facilitate a reflective debriefing [...] following the learners needs and objectives [...]*” (p. 3).<sup>275</sup>

Apart from applying a similar structure to the debriefing, revealing one’s stance and frames, and creating a safe learning environment, most experienced debriefers blend several debriefing models and conversation techniques and adapt them dynamically, depending on personal preferences, the learners’ perceived needs, and the scenario as experienced by the debriefer.<sup>275</sup> Asking open-ended questions in order to facilitate the discussion and foster self-reflection and self-assessment on the part of the participants as well as using silence after a question asked by the instructor are other key elements of facilitated debriefing.<sup>111</sup> During this silence, internal thinking processes on the part of the trainees are taking place. Open-ended questions cannot be answered with “yes” or “no” and therefore trigger the participant to explain the situation from his or her point of view. Some facilitators, especially when they are not highly experienced, use a debriefing script or a cognitive aid to help them lead the debriefing conversation effectively. On the other hand, sometimes the debriefer can just sit back and listen; the best debriefings may be when most of the discussion is purely between the participants themselves, addressing issues that are on target for the instructor’s purposes, in which case the facilitator will need to use very few specific techniques of debriefing.

For instructors, preparing for a good debriefing starts during the conduct of the scenario. A key skill for the debriefer is to be able to watch and listen carefully to what is happening in the scenario while also attending to the tasks of running it (Fig. 7.19).

For immersive, simulation-based team training, the debriefing sessions usually last approximately as long as the scenarios themselves, although a complex scenario may well generate a nuanced conversation that could go on for much longer. For shorter simulation activities, such as unannounced mock resuscitations, debriefings have to be much shorter. The number of debriefers can vary. Some prefer to have a single debriefer (or there may be only one

**TABLE 7.4**

Phases of debriefings: Issues relevant to (anesthesia) crisis resource management-based simulation debriefing.

The listed phases do not necessarily all have to be followed in this time sequence and order. Depending on the scenario, the participants' performance, and the debriefing format, several phases have to be repeated within the debriefing, especially during the debriefing center part, as indicated with the circle. Sometimes phases overlap when discussing the scenario.

PHASE OF DEBRIEFING	Explanation
Pre-Debriefing	Ending the scenario
	If possible, the (SC) should not be stopped too early. (P) should be allowed to realize the natural end of (SC). Ideally, (SC) should not be terminated when (P) are in the thick of it, e.g., still caring for the patient and applying treatment measures.
Scenario-to-debriefing transition	Most sites use debriefings immediately following the simulation. This allows the (I) to hear and see (P)s' direct reactions. A variant is to give the (P)s a few minutes to discuss the (SC) itself while the (I) is planning the (D).
Debriefing Start	Emotional venting
	All (HS) are given the opportunity to say how they <i>felt</i> during the (SC). This vents pent-up feelings and may be a time to deal with anomalies in the (SC) (e.g., simulator malfunction, simulation artifact, etc.).
	In this phase, (P)s also can critique the (SC)—critique that the (I) should acknowledge and take seriously.
	Descriptive phase
	(P)s describe what happened (or portions of the audio-video recordings are replayed) and what the clinical problem in the scenario was. Different points of view are shared (e.g., doctor vs. nurse vs. first responder vs. surgeon, etc.).
	Self-identification of issues
	It is sometimes useful to ask (P) to identify issues that did not go well or what they would do differently, in order to give them the opportunity to critique themselves before anyone else does. Nevertheless, the (I) can and should help identify what the underlying causes were and the pros and cons of alternate approaches.
Debriefing Center Part	Discussion of clinical content
	Any major issues of clinical treatment and related CRM points should be covered. A (D) should not end without discussing and clarifying any significant clinical errors and ensuring that participants understand the correct clinical management.
	Analysis
	(D) should provide considerable analysis of <i>why</i> things happened vis-à-vis the intentions of all parties, as well as alternatives and their pros and cons.
	Transfer to the "real world"
	Participants can discuss how lessons from the scenario or debriefing can be applied in the real clinical world. They should discuss barriers to improvement and ways to overcome them.
	Opportunities for systems improvement
	When applicable, based on the analyses, (P)s can be asked to suggest how the system can be changed to improve handling of similar situations in the future.
Debriefing End	"Take-Home-Message"
	A summary of the learned key points of the (D), either by (I) or (P), can be useful.
	Terminating the debriefing
	(D) are rich in content and easily can extend beyond the time available. Thus, giving a time frame for the (D) and officially marking its end is a useful transition to preparing for the next (SC) or the end-of-day activities.

"Hot Seats" (HS) = Participants (P) who were actively involved in the scenario (SC); Debriefing Room (DB); Simulation Room (SR); Simulation (S), Instructor (I), Debriefing (D), Crisis Resource Management (CRM).

Provided by M. Rall & P. Dieckmann as used in their own courses, derived from the original ACRM-course structure by D. Gaba and colleagues and used by many others around the world.

instructor) but often there are two or more "co-debriefers." Coordinating multiple facilitators can be tricky (it is sometimes described as being like dancing). Cheng et al.<sup>264</sup> described several effective strategies for co-debriefing.

Generally, faculty members intending to be debriefers in immersive simulation-based education need special training and practice in this teaching method<sup>105,119,238,282,283</sup>

and continuous experience and training throughout their career.<sup>275</sup> Several simulation centers conduct instructor training that emphasizes debriefing skills, and debriefing is a frequent topic of workshops at large simulation conferences.

**Box 7.6** shows a selection of the learning myths—especially in regard to the debriefing of patient simulation team



**Fig. 7.19 High workload for instructors during a simulation case.** The photograph shows the instructor team in front of the control panels and monitors in a control room during a simulation scenario. The control room is separated from the simulation room by a one-way mirror. The instructors have to operate the simulator, control the course of the scenario and the vital signs, give live in-scenario guiding, communicate with confederates who support the simulation in the scenario room, and at the same time take notes for the debriefing. These complex tasks need prior training or experience and good organization on the part of the instructor team. (Photograph by B. Schaedle, Momentum Photo at University Hospital, Tübingen, Germany.)

training—that seem to spread among medical educators, but are erroneous in the eyes of the authors, especially when training health care professionals.

### USE OF RECORDED AUDIO-VIDEO SEQUENCES IN DEBRIEFINGS

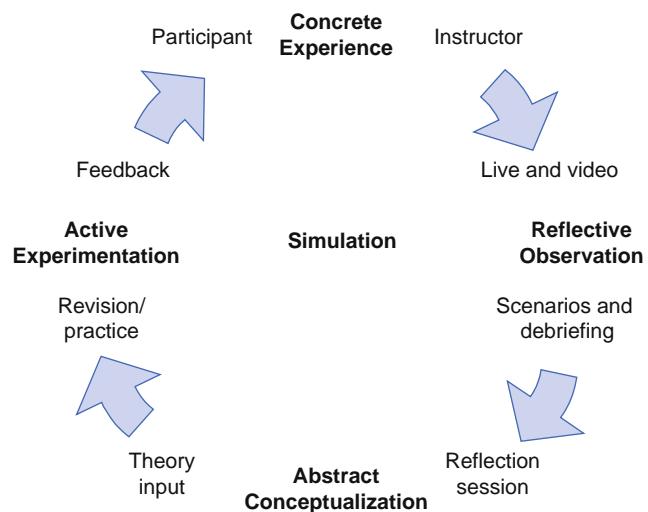
In the initial ACRM simulation courses the debriefer and participants viewed the entire recording, pausing at points for discussion. This practice has been abandoned and today most debriefers use the recordings only strategically to trigger discussion of specific points.<sup>111,119,202,283,284</sup> Studies of debriefing provide varying results as to the utility of showing the recordings and there is no definitive proof that this deepens the debriefing experience.<sup>116,118-120,285</sup> Nonetheless, snippets of audio-video recordings are frequently used as a learning and self-awareness experience.<sup>117,119,202,284</sup> Some studies point toward a positive effect, others do not. As the process of debriefing is complex and the effects of simulation and debriefing are expected to be a long-term accumulation of learning, reflection, and change, it is not surprising that teasing out cause and effect is difficult.

One argument for the use of audio-video-triggered reflection is that anesthesia does not support much self-reflection during routine clinical work. Experienced anesthesiologists often work alone, and there is often little feedback from other anesthesia professionals or from other operating room personnel. Most cases are followed as quickly as possible with the next. The lack of peer feedback leaves a large gap between the way individuals think they perform and how they act in reality. Based on the experiential learning cycle of Kolb<sup>286</sup> (Fig. 7.20) the opportunity to witness one's own behavior via a recorded audio-video sequence can be more meaningful to clinicians than described behavior criticized by the instructor. Another argument is that viewing the live transmission of the simulated scenarios is

### BOX 7.6 Erroneous Learning Myths in Simulation Training

**Learning Myth No. 1:** *“Participants always need to figure out themselves what they did wrong.”* Although self-reflection can be powerful, instructors can and should be ready to point out examples of problematic decisions or actions that are relevant to the clinical setting and to stimulate discussion of the alternatives and their pros and cons. This may lead to better understanding of possible solutions and how different clinical contexts will affect which are preferred. If participants grasp the situation and possible solutions on their own that is great. But if not, debriefers should not make participants search for the answer they wish to hear (this is called a “guess what I’m thinking” question); rather, they can use their own experience to suggest approaches that have worked for them.

**Learning Myth No. 2:** *“You always have to say something positive before you criticize.”* Educators describe the “sandwich” approach; the full sandwich has a filling of negative comment(s) sandwiched between two positive comments (a simpler “open-face” sandwich is also seen). Since debriefing is not “feedback” this is usually unnecessary. The discussion of what transpired and why should facilitate health care professionals learning from the analysis of all aspects of performance without special cushioning of the blows.



**Fig. 7.20 Kolb's experimental learning cycle.** Simulation team training with live video transmission and a debriefing with audio-video recordings demonstrates an ideal representation of Kolb's learning circle. During the scenario, actively involved trainees have a concrete “hands-on” experience. With the facilitation of the instructor and the own observation of audio-video sequences, the individual behavior can be actively reflected in the debriefing (“reflective observation”). The live video transmission to the non-active group during a scenario allows “reflective observation” during the scenario. During the debriefing, all trainees (active and non-active) have a phase of abstract conceptualization, in which the instructor uses generalizations of factors and root causes to show how behavior developed as it did in the scenario. With the instructor's theory input and the eventually triggered discussions, deep learning can take place and a plan can evolve during the debriefing, for both active and non-active trainees, of how to handle a similar situation next time. Active experimentation with the newly learned input and the drawn conclusions for the active as well as the non-active group can take place either during the next active scenarios or during real patient care. (Modified from Kolb DA. *Experiential learning: experience as the source of learning and development*. Englewood Cliffs, NJ: Prentice-Hall; 1984.)



**Fig. 7.21 Quad split monitor of a simulation exercise.** The quad split of a simulation exercise shows the vital signs during the scenario and usually three different camera perspectives during a simulation scenario. The quad split can be used for the live transmission of the simulation scenario to the participants who are not directly involved in the scenario. And it also serves for the later audio-video-based debriefing to reflect what happened in a certain situation, providing the advantage of different angles of view and an isochronic view of the vital signs. (Photograph provided by M. Rall, InPASS in-situ-training at Scuol Hospital, Switzerland, Chairman J. Koppenberg.)

useful for participants who are not actively involved in a given scenario (see Fig. 7.20 and Fig. 7.21). There is evidence that observers of simulations can learn as much as participants.<sup>287</sup>

Advanced simulation course formats generally closely reflect Kolb's circle of adult experiential learning: (1) self-experience (participate in the scenario) or vicarious experience (observe scenario live), (2) reflect on experience (debriefing), (3) abstract conceptualization (debriefing, relate to theoretical material), and (4) active experimentation (future scenarios and use of skills in real cases).

When live transmission is used as an alternative to just watching, the observers can be given special tasks (e.g., look for assigned CRM key points, see Box 7.4) so that they are more engaged in the process. Use of sequences of the scenario recording for debriefing requires additional instructor judgment and high proficiency controlling the replay system.

### EXCURSION: DEBRIEFING TECHNIQUES FOR DISCUSSION OF REAL CLINICAL CASES

Techniques of debriefing have also been applied to the analysis of real patient care events. Eppich and colleagues offer a guide to how this can be done in their article “*Let's talk about it*: translating lessons from healthcare simulation to clinical event debriefings and clinical coaching.”<sup>288</sup> Applying the debriefing techniques in short debriefing circles to involved clinical team has also proven quite valuable.<sup>245,276,289-291</sup> Clegg and MacKinnon<sup>292</sup> highlight in their paper “*Strategies for handling the aftermath of intraoperative death*” the need for a debriefing of the OR team after a critical incident in the OR and this concept is in accord with findings of other surveys.<sup>293</sup>

Debriefings after clinical cases can help teams learn.<sup>288,294,295</sup> This is particularly true for crews or action teams with short tenure and changing team membership

that have limited time to develop and learn as a team.<sup>296</sup> Here, debriefings offer a useful structure for learning because members may apply the lessons learned from a debriefing of one action team to teamwork of another action team.<sup>296</sup> The advantages of team debriefings include a reduced number of mistakes, higher levels of speaking up and performance, and shorter work duration.<sup>129,296-298</sup>

However, there are barriers to achieving effective debriefings for formative assessment after real cases.<sup>299</sup> For example, teams are typically uncomfortable with explicit communication,<sup>300</sup> they tend to discuss already known instead of new information,<sup>148</sup> and dynamics in organizations foster “undiscussable” topics.<sup>105,301</sup> For example, the various debriefing systems provide useful structures for debriefings after clinical cases, although their particular logistics may have to be adapted to the clinical setting.<sup>302</sup> Unfortunately, most post-clinical event debriefings lack an appropriate setting, a trained debriefing facilitator, and sufficient time.<sup>294</sup> For example, after a cardiac arrest, (1) when resuscitation is successful many of the team members come from the ICU, so they will be busy transporting the patient or otherwise caring for them; or (2) whether or not the event was clinically successful, team members may well have been called away from important activities that need their attention, severely limiting their ability to debrief.

### EXCURSION: DEBRIEFING TECHNIQUES FOR MORBIDITY AND MORTALITY CONFERENCES

Much of the philosophy and technique of debriefing applies to discussions of real cases such as morbidity and mortality (M&M) conferences. Both should be about exploring how and why things happened the way they did as opposed to the all-too-common emphasis on who was to blame. Both debriefing and M&M should aim not only to be educational for those participating but also to suggest ways to prevent or mitigate problems in the future, especially by correcting

systems issues. Overall, both aim to be constructive, not destructive.

However, both debriefing and M&M conferences face the problem of “hindsight bias” (see also [chapter 6](#)). After an event it is often clear what the problem was and how it could have been avoided or best treated, making the original clinicians look foolish. Hindsight bias is very hard to avoid but effort should be made to analyze events from the standpoint of the professionals on the spot in terms of the information they had available at a given moment. Gaba sometimes will explicitly say, “*unfortunately our crystal ball for seeing the future was not operating that day.*” Decisions that seem foolish in hindsight will often become totally understandable from this viewpoint.

Another common ground rule is to talk only about observable behaviors—the performance—not about individuals, personality, attitudes, assumptions, or interferences. If someone involved decides to disclose internal thoughts this can then become a topic of discussion. Using such philosophy and technique has a better chance of finding correctable systems issues, fostering a culture of safety, and making personnel comfortable in reporting and discussing problematic cases for the benefit of future patients.

## DEBRIEFING IN DIFFERENT CULTURES

While debriefing is widely recognized as an important part of simulation-based training, how it unfolds in practice depends on various contextual considerations. Many of the debriefing models stem from North America and Europe—what might be called the Western cultures. Arguably, the whole idea of debriefing—verbal reflective discussions of actions—might be seen as a Western idea. With simulation spreading more around the world, different national cultures, traditions, habits, and patterns of interpretations become more relevant.<sup>303</sup> The relationship between the learner and the instructor will be influenced by the general customs about how people of different hierarchy levels interact with each other. A recent study, based on interviews with experienced simulation instructors in 28 different countries, showed a strong relation between “power distance” of countries and specific patterns of behavior during the debriefing. The higher the power distance, the more important is the debriefer, the more closed questions are used, and the more difficult it is for participants to discuss issues of non-technical skills and speaking-up.

## Qualification and Certification of Simulation Instructors

It has been nearly 30 years since the first major wave of simulation in anesthesiology and other domains began. Over this time a variety of questions have surfaced, in general and at each institution, about how to create and sustain a cadre of simulation instructors. These include: (1) Do simulation instructors need special training? (2) Do they need continuous training after their primary training and if so how much and how often? (3) Do they need to be officially (re-) certified periodically? (4) How can the quality of an instructor be measured or differentiated? This section addresses these questions.

## TASKS OF SIMULATION INSTRUCTORS—LEARNING OBJECTIVES FOR SIMULATION INSTRUCTOR COURSES

Sometimes, simulation teaching is completely analogous to bedside teaching, only with a simulated patient, and all the same skills apply. For other uses of simulation new skills may be needed,<sup>112,272,299,304</sup> especially for simulation activity that involves: (1) complex realistic scenarios, (2) with multiple personnel in crews and teams, (3) conducting debriefings in small groups (with or without video), (4) with a focus on human factors and CRM principles and feasible countermeasures. It is widely thought that the quality of the instructors is *the* essential element for any simulation training course, and for complex activities their competence as debriefers is the primary aspect of quality.

Most clinical educators do not necessarily have the skills most needed to be a fully capable simulation instructor. The key tasks include:

- Create relevant, plausible, meaningful clinical scenarios with the necessary realism to reach the intended learning goals (although some instructors who are excellent debriefers leave the design of scenarios to their colleagues).
- Establish an engaging learning context.<sup>121</sup>
- Brief/familiarize simulation participants about the simulator and the unfamiliar simulation environment.<sup>121,299</sup>
- Conduct (complex) clinical scenarios with the need for simultaneous control of (1) the simulator, (2) the simulation environment (i.e., in-scenario information,<sup>261</sup> etc.), (3) the simulation personnel (co-instructors, role-players, simulation technicians, etc.), and (4) the real-time adjustment of scenarios to offer optimal learning for all participants.
- Provide a structured post-scenario debriefing and feedback stimulating self-reflection, facilitating peer-discussion, creating deep and sustainable learning, and promoting transfer lessons to the real world.
- Act on adult learning principles, balancing facilitation and instruction during debriefing (i.e., Kolb’s experimental learning cycle, see [Fig. 7.20](#)).
- Handle, as necessary, group dynamics as well as individual sensitivities during the training and the debriefing.<sup>272</sup>
- Use recorded audio and video strategically to facilitate debriefing (and/or for feedback especially about technical or procedural skills).
- Teach about crew resource management (CRM) decision making, situation awareness, task and team management, communication, and professionalism in addition to the transfer of medical knowledge.
- Highlight system optimization based on system theory principles of patient safety.

## EDUCATION, TRAINING, AND CONTINUOUS DEVELOPMENT OF SIMULATION INSTRUCTORS

### Instructor Education and Training

As described by Fanning and Gaba,<sup>238</sup> unlike a traditional teacher, the facilitators can position themselves not as an authority or expert, but rather as a peer and co-learner. Oftentimes, especially for experienced medical teachers,

### BOX 7.7 Learning Objectives for Crisis Resource Management–Oriented Simulation Instructor Courses

- Understand how it feels to be a participant in a simulation scenario
- Understand how it feels to be debriefed in a group while others are watching or while seeing oneself on video
- Understand the interdependent influences of the different course phases (“anatomy of a simulation course,” see Fig. 7.18) and apply this knowledge to a simulation exercise or course
- Reflect on the changing instructional styles that can be applicable to simulation courses (instruction versus facilitation)
- Understand basic concepts of human factors, crisis resource management (CRM), systems theory, and organizational safety (see Chapter 6)
- Be able to detect, explain, and discuss CRM key points during the debriefing of scenarios
- If using video sequences, use recorded video clips of scenarios well, and select the most relevant portions for replay and discussion
- Be able to conduct a structured debriefing and facilitate a debriefing in a nonjudgmental atmosphere with appropriate boundaries
- Understand how to manage the individual sensitivities and group dynamics of participants during debriefing
- Instead of discussing “who” made “what” “mistake,” be able to focus debriefing on the analysis of “what happened,” “why did it happen the way it did,” “what lessons can be learned,” and “how to apply these lessons to real patient care”
- Create a well-designed scenario with learning objectives appropriate for the population

Modified from the learning objectives of instructor courses by Gaba, Rall, and Dieckmann.

the most difficult task in learning this teaching approach is to stop lecturing and start listening and facilitating. At the same time, providing honest critique while holding the learner in high regard—what the authors call “critiquing the *performance* not the *performer*”—seems particularly challenging.<sup>106,304</sup> This is, among other things, why simulation-based educators usually need special education and training. **Box 7.7** presents an example of learning objectives for an instructor training course.

Gaba, Howard, and Williams from Veterans Affairs Palo Alto Health Care System /Stanford School of Medicine (VAPAHCS/SU) pioneered CRM-oriented simulation instructor training in 1992, taking their homemade simulation system to Boston for 3 months and teaching approximately a dozen faculty of the Harvard Hospitals anesthesiology programs how to conduct ACRM courses. A few years later a consortium of the Veterans Affairs Palo Alto/Stanford (VAPAHCS/SU), the Boston Anesthesia Simulation Center (the forerunner to the Center for Medical Simulation), and the University of Toronto Sunnybrook Simulation Center created a formal instructor course, spreading the ideas and format of CRM simulation instructor training around the world. Rall has run instructor courses in cooperation with Dieckmann for more than 3000 international participants. Many institutions now offer different instructor courses nationally and internationally (ranging from 2 to 6 days in length, depending on the course and its scope). For further information about such courses the reader is referred to the simulation societies such

as SSH or SESAM, or Internet searches targeting well-known simulation centers. In addition, shorter introductory courses on instructor skills are offered every year at the international health care simulation meetings (e.g., SSH’s IMSH conference, or the SESAM annual meeting); many workshops at these meetings cover topics such as debriefing, instructor training, and CRM training.

### Continuous Faculty Development

Recent research demonstrates the variety of challenges simulation educators perceive when conducting simulation-based training sessions.<sup>272,304</sup> For example, debriefings can include difficult situations such as learners who are unusually quiet, disengaged, or overwhelmed by emotions.<sup>272</sup> Faculty development is important to prepare simulation educators to design and conduct meaningful and respectful training sessions while anticipating potential problems, intervene proactively, and when necessary manage them with good sense and grace.<sup>272,305</sup> Since debriefings are considered particularly challenging, special emphasis is given to continuously improving these skills.<sup>106,306–308</sup>

Reflection can help simulation faculty identify how to improve their debriefing skills.<sup>304</sup> Observation of master debriefers, interactive learning experiences, practice, feedback by peers and experts, and mentoring can foster such improvement.<sup>309–311</sup>

Valid and reliable tools such as the Debriefing Assessment for Simulation in Healthcare (DASH)<sup>307</sup> and Objective Structured Assessment of Debriefing (OSAD)<sup>312</sup> can be used to monitor debriefing quality and provide data for feedback conversations for faculty development. DASH is available in a variety of languages (to date, English, German, French, Japanese, Spanish; <https://harvardmedsim.org/debriefing-assessment-for-simulation-in-healthcare-dash/>). DASH consists of six rating elements: (1) setting the stage for an engaging learning environment, (2) maintaining an engaging context for learning, (3) structuring the debriefing in an organized way, (4) provoking an in-depth discussion which allows for reflection, (5) identifying performance gaps and their reasons, and (6) helping to see how to improve or sustain good performance. The OSAD consists of eight categories: (1) approach, (2) environment, (3) engagement, (4) reaction, (5) reflection, (6) analysis, (7) diagnosis, and (8) application. Both tools can be applied from various perspectives (i.e., learners, colleagues, educators) which allow for a multifaceted view on debriefing quality.<sup>313</sup>

### CERTIFICATION OF SIMULATION INSTRUCTORS

Since being a simulation instructor often requires special skills it is almost universally true that only a small fraction of an institution’s faculty or staff are involved in this. For very long-standing simulation groups and centers, informal internal mechanisms have often been used to select and approve instructors. For the bulk of simulation groups and centers there has long been a desire for some formal professional recognition of who is qualified to develop, conduct, and/or debrief health care simulations which has led to different models of certification of qualified individuals. One model is that of the Academy of Medical Educators (AoME),<sup>314</sup> a UK-based organization of educators of medical, dental, or veterinary professionals, for which

membership requires satisfying certain levels of achievement in the following five professional standard domains:

- Designing and planning learning
- Teaching and facilitating learning
- Assessment of learning
- Educational research and scholarship
- Educational management and leadership

For each domain, three levels are available that allow assessment and documentation of progress of a person. For more information the reader is referred to the AoME website (<https://www.medicaleducators.org/>).

The SSH offers a model that addresses more of the simulation-specific aspects of the educator role, and is applicable to all personnel, not just “medical” educators. There is a basic and an advanced level of certification. For more information about the certification for Certified Healthcare Simulation Educator (CHSE) and the Certified Healthcare Simulation Educator—Advanced (CHSE-A) the reader is referred to the society’s webpage (<https://www.ssih.org/Certification>). These programs are rather general and do not fully address the details of qualifications applicable to specific courses. SSH certification has been far more popular for nursing personnel than for physicians; this probably accounts for the fact that few simulation instructors in anesthesiology have obtained formal certification. In another approach, while the U.S. ASA Simulation Education Network (SEN) program endorsement process does not yet certify instructors, when considering a site for endorsement it does examine the simulation background of the site’s instructors, as well as the process by which each site trains and approves new instructors for their program.

It is likely that the skills and certification needed (if any) for an instructor will vary greatly with the particular course or curriculum being taught. Competence in conducting a video-based CRM debriefing would not be needed, and would not help, to teach specific manual procedures (e.g., airway management or central venous cannulation) using part-task trainers. Some sites use either a formal or informal system of tiered instructor categorization tied to the specific types of courses and roles each individual is capable of conducting. This also provides a defined process for advancement from novice instructor to grand master as experience and special training are acquired.

## Accreditation of Simulation Programs, Sites, and Centers

Besides the qualification of the instructors, the physical and organizational infrastructure is important for the quality of simulation in health care. This aspect is discussed under the label of accreditation. The SESAM wrote: “*By seeking accreditation an institution can demonstrate its quality as having been judged and validated by an independent body who is internationally recognized as an opinion leader in the domain of simulation-based education in healthcare.*”<sup>315</sup>

Several systems of program approval have emerged, some of them of particular interest to anesthesia professionals.

SESAM provides a model that has two levels of accreditation ([www.sesam-web.org/accreditation/](http://www.sesam-web.org/accreditation/)). The basic level is done based on the description of the program’s work; the expanded level also includes a site visit.

### BOX 7.8 Simulation as Favored Option for Part IV of the U.S. Maintenance of Certification in Anesthesia Program by the American Board of Anesthesiology

The simulation course must be held at a site endorsed by the Simulation Editorial Board of the American Society of Anesthesiologists, with a curriculum meeting minimum standards. Although not specifying anesthesia crisis resource management (ACRM) directly, the standards for the U.S. Maintenance of Certification in Anesthesia (MOCA) simulation are clearly derived from the ACRM simulation courses that have become common around the world:

- A minimum of 6 h of total course instruction
- Active participation in realistic (mannequin-based) simulation scenarios
- Post-scenario instructor-facilitated peer debriefing
- Management of difficult patient-care scenarios, including at least scenarios involving the following: (1) hemodynamic instability and (2) hypoxemia of any cause, including management of the difficult airway
- An emphasis on teamwork and communication
- All participants have at least one opportunity to be the primary anesthesiologist in charge (i.e., the “hot seat”)
- The participant-to-instructor ratio must be no greater than 5:1
- At least one instructor must currently be in the MOCA process

The SSH provides an accreditation program, with separate but related accreditations for core standards plus one or more of the following areas of emphasis: teaching/education; assessment; research; systems integration. For more information, the reader is referred to their webpage (<https://www.ssih.org/Accreditation/Full-Accreditation>).

The U.S. ASA has a process to endorse anesthesia simulation programs (the ASA chose not to use the term accredit) qualifying them to be members of the ASA’s SEN. Centers were originally endorsed for their ability to deliver high-quality CME to ASA members. After reaching agreement with the ABA in 2010, this ASA SEN rapidly transformed into a group of programs capable of conducting the semi-standardized Maintenance of Certification in Anesthesia (MOCA) Simulation Course. The course is a component of Part IV (practice improvement) of the ABA MOCA process. **Box 7.8** shows the features of the U.S. Maintenance of Certification in Anesthesia (MOCA) simulation program.

As of November 2018, the ASA had endorsed more than 50 programs, each of which was reviewed and approved by the ASA Simulation Education Editorial Board after completion of a detailed application documenting the capability and experience of their simulation instructors, leadership, facilities, and procedures (for ASA members, see <http://www.asahq.org/For-Members/Education-and-Events/Simulation-Education.aspx>).

The American College of Surgeons (ACS) has a program of Accredited Education Institutes (AEI) that “...educate and train practicing surgeons, surgical residents, medical students, and members of the surgical team using simulation-based education.”<sup>316</sup> Many anesthesia simulation programs, especially those endorsed by the ASA-SEB, have a close collaborative relationship with their institution’s ACS-AEI.

## Benefits, Effectiveness, and Ecological Validity of Simulation Training

In the era of evidence-based medicine everyone wants to know “does simulation work?” and “what is its cost effectiveness?” This question has now been answered affirmatively, but only for a selected few circumstances. In fact, it seems clear that for many of the common, but most challenging arenas of health care, these questions may not be answerable for all practical purposes.<sup>317</sup> Some argue that the question of whether simulation works needs to be replaced by questions about “when,” “how,” and “under what conditions” simulation “works,” and finally “how ‘works’ can be defined” in a given context. In the following, the benefits of simulation are summarized, and some challenges to answer the above raised questions as well as some key findings in settings in which studies were feasible are reviewed.

### BENEFITS

Simulation in health care has some fundamental advantages as a training tool. The following were modified and expanded based on the work of Gaba and DeAnda<sup>177</sup>:

- No risk is posed to a patient despite “hands-on” training.
- Routine clinical situations, emergency situations, and those involving uncommon but serious problems can be presented at will.
- Participants can learn to use actual complex devices, often in the relevant clinical context.
- The same situation can be presented independently to multiple subjects for evaluating individual or group performance.
- Errors can be allowed to occur and play out to their likely conclusion, whereas in a clinical setting they would require immediate intervention by a supervisor.
- To a reasonable degree, the training can be standardized and is reproducible.
- Training can be focused and allows for various forms of feedback or discussion that are difficult to embed into real patient care settings.
- “Clinical time” is under the control of the instructor; boring portions can be skipped or sped up while very difficult segments can use time dilation to allow unfamiliar individuals to have a full chance to grasp and handle the situation.
- Simulation can be stopped and restarted for teaching; time of physiological changes can be expanded or compressed, including “death-control.”
- Recording, replay, and critique of performance are facilitated because patient safety or confidentiality is not an issue.

Simulation accelerates skill acquisition, improves skill retention, and reduces the extinction of skills.<sup>26</sup> Simulation has been heavily utilized to address non-technical skills (see Chapter 6) such as communication, teamwork, task management, leadership, situation awareness, and decision making. Those non-technical skills and human-factor-based training approaches are vital to conduct safe patient care, taking into account human performance

strengths and weaknesses (see Chapter 6). Nevertheless, as mentioned below, such an arena will be the hardest to ever prove that simulation improves patient outcome.

Despite the many advantages of simulation in health care adverse effects of simulation are possible. A stimulating critical overview of medical education in general was written by Hodges and was provocatively titled “*Medical Education and the maintenance of Incompetence*.<sup>318</sup> The article points out that any type of education runs a risk of creating or maintaining incompetence in certain areas, especially areas that are ignored by the actual educational program. The authors recommend that all simulation instructors be especially cognizant of the risks that Hodges articulates.

### EFFECTIVENESS

**Challenge #1: Comparability of simulation research and evaluation of simulation.** For the question of whether simulation works and how effective simulation is in regard to different aspects, evaluation concepts need to be defined and a common ground for the comparison of research in simulation needs to be produced. For the evaluation of learning and later performance outcomes, respectively, oftentimes the four-level model of Kirkpatrick as shown in Fig. 7.22 is cited.<sup>319,320</sup>

Another concept used to evaluate simulation is that of translational science—research designed to accelerate movement of results from the laboratory bench to the patient bedside. The concepts of a continuum of research from fundamental science through clinical trials to widespread use in patient care and of potential translational blocks were articulated originally by Sung and colleagues in 2003.<sup>321</sup> From this publication emerged various nomenclatures for the different levels of the research continuum in terms of increasing level of translation, called T Levels.

For education, translational science addresses how results achieved in the educational laboratory (T1) transfer to improved downstream patient care practices (T2) and improved patient and public health (T3).<sup>322</sup> McGaghie<sup>322-324</sup> first adapted the T levels of translational research to the arenas of medical education and simulation in health care, comprising T1, T2, T3, and T3' (Table 7.5). The most important T levels for simulation interventions are T1: is performance improved when observed during simulation?; T2: does actual clinical behavior change in the workplace?; T3: is there a change in patient outcome?; and to a lesser extent T3': is it cost-effective?

Based on those two concepts, for research purposes simple outcomes are Kirkpatrick level 1 (reactions of participants) and Kirkpatrick level 2 (change in self-confidence or of knowledge measurable via multiple choice questions). Both Kirkpatrick levels are represented by level T1. Rall et al.<sup>325</sup> later adapted additional T levels mentioned in other sources,<sup>326,327</sup> adding levels of T0, T4, T5, and T6 (see Table 7.5), and categorizing interventions by their intended outcomes. Researchers in simulation are now starting to use this terminology in describing and comparing their research protocols and results.

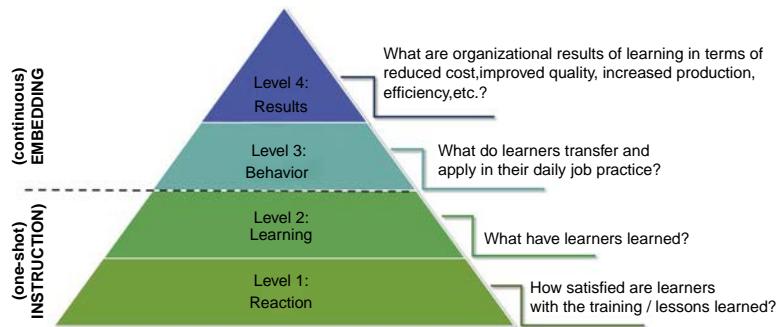


Fig. 7.22 Kirkpatrick's four-level training evaluation model. The model is composed of four levels: reaction—learning—behavior—and results.

**TABLE 7.5** Translational Research Levels of Simulation-Based Training

Level	Description of Study Methodology	Comments/Examples
0	No measurement of learner performance	Questionnaire or multiple-choice test to assess reaction/change in knowledge
1	Performance measured during simulation only	Do participants do better in a subsequent simulation?
2	Performance measured during actual clinical care	Do participants do better in subsequent clinical practice?
3	Measurement of improvement in patient outcome	Do patients of those who had the training fare better?
3'	Measurement of cost of the intervention, the outcome, and the monetary benefit (= measuring "cost effectiveness")	Does intervention yield a net saving of money (with/without improving outcome)?
4	Measurement of dissemination of the intervention to sites beyond trial sites	Has the intervention spread elsewhere successfully?
5	Measurement of adoption of the intervention in regular practice	Has it been widely adopted?
6	Measurement of population health outcome	Has it made an impact on patient population as a whole?

**Challenge #2: To define cost-effectiveness, expenses need to be put in context relative to return on investment.** In simulation education the focus of evaluations historically has been mostly on qualitative instead of quantitative measures, and the suite of measurements needed to assess learning outcomes and patient outcomes are still in flux. Bukhari and colleagues published a framework for determining the return on investment of simulation-based education in health care.<sup>328</sup> Unfortunately, so far, evaluations that yield economic information about the return on investment are scarce.<sup>329</sup> And the expenses (see later section) vary (high cost to low cost) depending on many choices regarding the setup of the simulation training (see earlier section on “12 Dimensions of Simulation”).

At this point, most studies of simulation-based learning are at level T0 or T1. At lower T levels simulation of various sorts has been shown to have small to medium positive effects.<sup>330</sup> A few studies have been at T2 and only a handful at T3 or T3' patient outcome. Draycott and colleagues<sup>331</sup> showed positive effects of training that included some simulation components on neonatal outcome. Barsuk and colleagues<sup>126</sup> showed a reduction of central line complications and cost-efficacy after implementing simulation-based training on central venous cannulation. A series of studies from Tanzania shows that positive effects for patients is not necessarily related to the use of high-end simulation equipment.<sup>38,332</sup> Van de Ven and associates<sup>333</sup> concluded in their study that multi-professional team training for obstetric emergencies in a

medical simulation center is cost-effective in a scenario where repetition training sessions are performed on-site. Levels T4 and T5 can be considered implementation science, but few studies of simulation implementation have been performed.

Simulation researchers are encouraged to move toward studies at higher levels of translational research whenever possible. Admittedly, the cost and complexity of studies also rises non-linearly as one climbs the “T ladder.” Since many applications of simulation in anesthesiology especially focus on preparing anesthesia professionals to prevent and manage uncommon but serious adverse events more effectively, the rarity of such events and the many confounding variables that affect patient outcome will make intervention studies very difficult to perform.<sup>317</sup>

These studies would per force need to be large, long, and complicated. To date, almost all studies have been too short and too unsystematic, with weak interventions and without adequate control of confounding variables. Unlike many types of clinical trials, which are funded by the pharmaceutical industry—which is willing to invest heavily even in complex trials because of the high direct payoff when a blockbuster drug is found—simulation interventions have no equivalent funding sources. Obtaining level 1A evidence—with multiple randomized controlled trials—of simulation’s impact on patient outcome may well take studies of thousands to hundreds of thousands of patients, cared for by hundreds or thousands of clinicians, with simulation interventions that

are powerful, comprehensive, sustained, and linked to performance assessment (and remediation) of individual clinicians. As yet, no agency or commercial firm is willing to fund these kinds of large, long, and complex studies.<sup>317</sup> And neither aviation nor nuclear power have assembled “level 1A” evidence that simulation saves airplanes, power plants, or lives. It is unlikely that aviation would ever attempt randomized trials and such studies would be nearly impossible, if not unethical.

### **Challenge #3: High-fidelity patient simulations can be effective and cost-effective, but work will be educationally effective only, if they meet certain criteria.**

Flanagan and associates provided a thorough review of the literature on the efficacy of simulation-based training for learning and assessment.<sup>334</sup> They concluded that “simulation makes a valuable contribution to learning for students, trainees, and clinicians. It enables learning of both routine and non-routine procedures and management of patients.” In one study the effect between hours of simulation practice and learning outcomes equaled a dose-response relationship.<sup>198</sup>

Similarly to Flanagan, Cook and colleagues<sup>330</sup> concluded in their comparative review that simulation was typically more expensive but also more effective. In their summary, in comparison with other instructional methods, technology-enhanced simulation was associated with small to moderate positive effects. In another comparative review by Cook et al.<sup>335</sup> in which technology-enhanced simulation training in health professions education was compared to “usual practice,” simulation was consistently associated with large effects for outcomes of knowledge, skills, and behaviors, and moderate effects for patient-related outcomes. Such findings were confirmed by Lorello et al.<sup>15</sup> in their most recent review; they and other authors<sup>198,334</sup> pointed to the heterogeneity of the studies, the sometimes limited robustness of their methods, and the occasional lack of a suitable control group.

A Best Evidence in Medical Education review by Issenberg and colleagues concluded that high-fidelity medical simulations are educationally effective, but only if the following conditions are met<sup>198</sup>:

- Educational feedback is provided.
- Repetitive practice is used or is allowed.
- Simulation is integrated sensibly into the standard curriculum.
- The range of task difficulty can be adapted to the level of the learner.

### **Challenge #4: Limitations of research on simulation effectiveness.**

Even the strongest of results come with caveats. First, it can be difficult to isolate the effects of simulation in the evaluation. In many cases simulation is only a part of a larger bundle of interventions, or concurrent with improvements in the clinical field as a whole (“secular change” as statisticians say). Second, as in the case of central venous cannulation, sometimes the clinical activity is circumscribed, the outcomes are relatively common, there is already ongoing surveillance for them, the relationship of the activity to negative outcomes is well-understood, and the intervention is itself narrow, proving an effect on patient outcome is easy. But for many arenas, especially for the anesthesia professional’s management of unexpected adverse situations, the

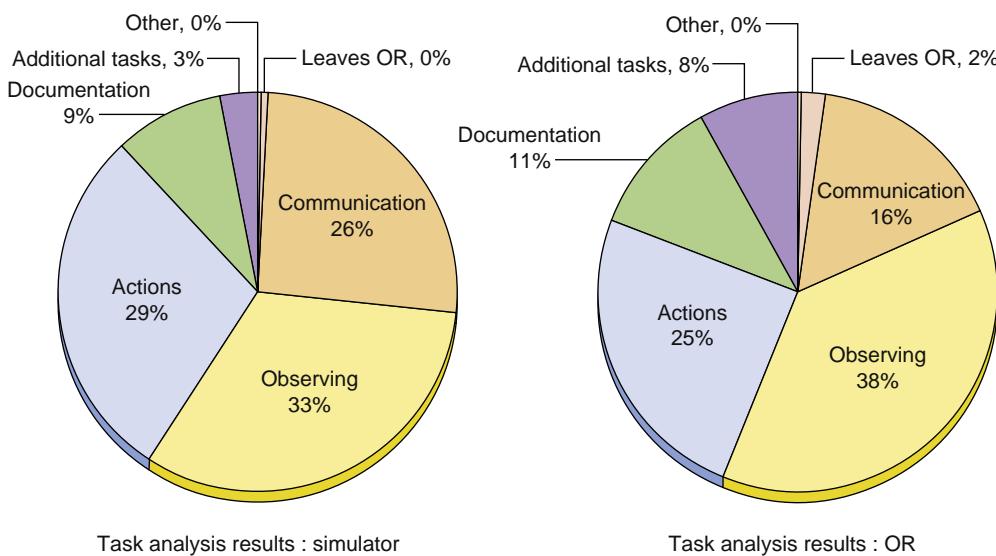
events are relatively rare; there is weak surveillance for negative outcomes, as well as many confounds between anesthesia professionals’ actions and the final outcome; and the simulation interventions are complex. Proving an outcome improvement is difficult in such settings and likely would require long, complex trials involving many tens or hundreds of thousands of patients, thousands of clinicians, and a very long time horizon, as mentioned above. Further, it is unrealistic to expect that a single set of training can change complex behaviors and actions or affect patient outcome especially when there is little reinforcement in or linkage to performance assessment in actual clinical practice.

### **Challenge #5: Assessing the impact of simulation in health care as if it was a pharmaceutical.**

The assessment of the impact of simulation to date can be seen using the following analogy to drug development and testing that was introduced by Weinger<sup>336</sup> and expanded to address the related policy issues by Gaba.<sup>317</sup> Suppose one wished to test whether a purported antihypertensive drug actually succeeded in reducing blood pressure in patients and, more importantly, whether it reduced the occurrence of adverse cardiovascular events, such as myocardial infarction and stroke. Imagine then that one proceeds as follows: administer a relatively small dose of this drug only a few times per year. Acknowledge variable compliance in taking even these few doses of drug. Immerse all subjects in an environment full of stress and other factors predisposing to cardiovascular events. Use only a few patients, and follow them for a very short time.

Would anyone wonder if no significant effect was found even for a drug otherwise known to be effective? Simulation in health care has so far been tested in this way: very small, short-term studies of infrequent (often short) simulation sessions, whose lessons are not fully reinforced in real clinical environments full of production pressure and stress. In truth, the question is not “*Does one run through a simulation course make a practitioner better?*” To follow the lead of other industries of intrinsic hazard, such as commercial aviation or nuclear power production, the question is “*What is the impact on health care as an industry adopting a comprehensive integrated strategy of intensive simulation-based training and continued performance assessment of clinical personnel, over a long period of time?*” This is the approach in aviation, in which no matter how senior and how experienced pilots are, they still undergo training and assessment in simulation every year, for the entirety of their careers.

It seems unlikely that pilots would forgo simulation training and assessment when their own lives are on the line. For another thing, the public has come to expect a regulatory safety floor imposed by the government to ensure the competence of pilots. The regulator is unlikely to forgo its requirement for mandatory training and testing of pilots. If such requirements continue, there may be only two options: conduct these exercises in real airplanes, with the attendant costs (e.g., fuel) and risks; or conduct them using simulation. With health care heading in that direction,<sup>92,222,226,245,337,338</sup> one may be able to assess the impact of more effective simulation programs, although one may lose a control group that has never experienced simulation.



**Fig. 7.23 Ecological validity of simulation versus the operating room (OR).** For study purposes<sup>160</sup>, the same anesthesiologists were observed in the OR and in the simulation environment with full enactment of the OR personnel, surgical team, and anesthesia nurse. Even though the two settings have some interesting differences, the overall ecologic validity of the simulation is good. (Courtesy of T. Manser, ETH Zurich, and University Hospital, Tübingen, Germany.)

Other industries have a career-long set of simulation interventions that are considered to have a cumulative effect on ability. Social psychologists Helmreich and Foushee, two of the main architects of CRM training, wrote: “Data indicate that even intensive initial CRM training constitutes only an awareness phase and introduction to the concepts, and that continuing reinforcement is essential to produce long-term changes in human factors practice.”<sup>339</sup> Similarly, United Airlines states in its CRM manual: “Command/Leadership/Resource management [United’s terminology for CRM] cannot be a one-shot approach. It has to be a coordinated long range program. It must therefore be an integral part of the entire training effort: new hire training, transition and upgrade programs, and recurrent training.”<sup>340</sup>

### ECOLOGICAL VALIDITY OF PATIENT SIMULATION: IS THERE TRANSFERABILITY TO THE REAL WORLD?

When trying to translate behavior of professionals in the simulation to the behavior professionals might show during real clinical cases, one of the questions raised is the one about whether simulation can engage trainees the same way a real clinical case would. Simplified, in psychological science this is referred to as ecological validity. If actions and behavior in the simulation resemble the actions and behaviors in real-world clinical environments, it is likely that the results of research conducted in a simulation setting or lessons learned in a simulation training will be transferable to the context of actual patient care.

**Patient simulation: A valid representation of the clinical reality?** The question whether full-scale simulations are a valid representation of the real work environment tasks (e.g., tasks of an anesthetist in the OR, etc.) was investigated by an interdisciplinary research group in Tübingen, Germany and Zurich, Switzerland.<sup>160</sup> Each of the six anesthesiologists participating in the study was

observed during two clinical cases and during three comparable simulator cases (one routine and two involving critical incidents). Analysis of the study showed good comparability of the different action categories as shown in Fig. 7.23. The interpretation of the group was that overall comparability between the operating room and the simulator setting is good, thereby indicating high validity for simulators in anesthesia.

Another more recent study by Weller and associates<sup>341</sup> examined the validity of the simulated environment with the question of whether anesthesia professionals show similar verbal communication patterns during a simulated and a real case. Seventeen anesthetists were observed via video-recordings during real cases and two simulated cases. Confirming the findings mentioned by the group in Tübingen and Zurich, the authors of the publication found no significant differences in communication patterns in the OR and the routine simulations. The participants themselves rated communication as realistic and considered their communications occurred with a similar frequency in the simulations as in comparable cases in the OR.

Those findings support the validity of the simulation environment and its value for transferable training and provide further objective confirmation of the favorable subjective impressions of realistic simulation scenarios by anesthesiologists of varying levels of experience.<sup>65,68,69,178,179,181,342</sup> Therefore, the evaluations presented in this chapter suggest that simulator-based training is a powerful technique that novice and experienced anesthesiologists believe to be highly beneficial, and that participants and instructors alike believe may improve clinical performance. As the developers of Sim One<sup>175</sup> pointed out, when simulation provides an opportunity to teach material that cannot be taught in another way, as for the systematic instruction of anesthesiologists in handling severe critical events such as cardiac arrest, anaphylaxis, or malignant hyperthermia, there is nothing with which to compare the simulator.

### Simulation replacing clinical hours or case numbers during training?

Because simulation offers a valid representation of real health care settings and behaviors, and also offers several advantages, in settings for which a certain number of clinical hours or patient cases are a prerequisite for certification or credentialing, simulations are sometimes allowed to replace some portion of the requirement. This is true in some states in Germany for prehospital emergency physicians (and possibly soon [pilot project] for paramedics) who are allowed to cover 25 of 50 mandatory prehospital cases within a specific 3-day simulation program.

For nursing, in the United States, 22 states allow some degree of simulation replacement of clinical hours required for final licensure as a registered nurse; the number or percentage of hours varies widely as does the specificity of the regulation and whether there are any standards for the intensity or quality of the simulation activities (see <https://www.inacsl.org/sim-regulations/>). A large and complex study of educational outcome (not patient outcome) provided evidence to support these practices,<sup>343</sup> although from Gaba's view there were some limitations concerning study methodology and the generalizability of the results.

### Differences between simulated and real-world cases.

Even though the mentioned studies showed high ecological validity of patient simulation, some differences between simulation and real patient care are inherent to simulation and need to be taken into account when debriefing and assessing the performance during a simulated scenario. Based on the findings of Manser and colleagues<sup>160</sup> variations were mostly the result of organizational factors (e.g., fewer additional tasks required in the simulator). At the same time, as described in the literature,<sup>75</sup> subjects (1) eventually become hypervigilant realizing that they are in a simulation, being more attentive or even doing more than they usually do (e.g., participants neglect documentation in the simulation while waiting for a disaster to happen, or scan the patient's documents at length before starting a simulated case so as not to miss an important hidden hint, or jump too quickly on signs of possible trouble); (2) conversely, will not or cannot take the situation serious because it is not a "real patient" and thus do not perform all the actions as they would for a real patient (e.g., acting sloppy, showing cavalier behavior, acting like it is a game).

Careful and creative scenario design and scenario conduct as well as proper introductory briefings may mitigate some of those effects (see earlier sections on those topics).<sup>273</sup>

## Cost of Patient Simulation and Simulation Centers

### COST OF PATIENT SIMULATION

An important question concerning simulator-based training in anesthesia is its cost effectiveness. This complicated question has two independent components. The first pertains to the impact and benefit of the training on the performance abilities of participants and patient outcome (discussed above), and the second is the cost to achieve that impact.

Although measuring the cost of simulation-based training depends on many factors, the cost may still be more easily estimated than is the impact of the training. Factors affecting the cost include:

- The type (or spectrum of types) of training involved
- The target populations for the training
- And perhaps most importantly, a variety of aspects of the organizational and financial structures and processes of the institution

The cost of simulation hardware and software varies greatly (and much simulation can be done with little to no technology). Screen-only simulators cost very little (a few hundred dollars), whereas the equivalent cost of a complete mannequin-based simulator or VR system is much higher. The price of a commercial mannequin-based simulator ranges from approximately \$25,000 for intermediate-capability simulators to more than \$150,000, depending on features; only the manufacturers can provide detailed information. This cost does not include any relevant clinical equipment (which, say, for an anesthesia machine is very high) and also of course the building and maintenance of a center's space.<sup>344</sup> Even these large expenditures do not dominate in the operational cost equation, however, because the construction cost is often borne by the institution itself, capital equipment can sometimes be donated or acquired used, and in general is amortized over a relatively long useful life, with appropriate provisions for service and upgrades.

The overall dominant cost for operating a center is likely to be the salary and benefits of its permanent personnel and the effort of expert instructors (which is typically borne directly or indirectly by their clinical department). These costs vary considerably across the spectrum of simulation activities and institutional arrangements. Usually an expert must oversee the curriculum (which may or may not impose direct costs), but the type of training and the target population will determine the amount of expert instruction required. A single faculty member can review the summaries of exercises performed by residents on a screen-based simulator in a few hours per resident per year. Non-physician instructors may be suitable for some task training or for drill and practice sessions. A single instructor can use the simulator to show pulmonary or cardiovascular physiology to a whole class of medical students. For training novice residents in basic anesthesia skills, it may be possible to have senior residents or fellows conduct the sessions at a low marginal cost. For training experienced residents and practitioners in complex material, such as the handling of critical events, it is likely no substitute expert instructors exist. The cost of expert instruction depends on the organizational arrangements of the institution. In a teaching institution where faculty members all have at least some time allocated for teaching or scholarly activities, some faculty may choose to fulfill this requirement by simulation-based teaching or scholarship. When further instructor effort is needed, payment—by the department or the center—for clinical release time may be needed.

Another organizational cost factor relates to providing access to participants for what can be complex, exhausting, and lengthy training sessions. Removing clinical personnel from revenue-producing work for training purposes is

expensive. If simulation training could allow them to work more safely and efficiently, the benefit could outweigh the cost. Some research indicates that simulation team training can improve job satisfaction and effectiveness of routine care, as well as contributing to reduced illness leave and job fluctuations.<sup>345</sup> Some residency programs provide protected time for education of residents (e.g., one half day per week). In such cases, residents should already be available for simulation, but it might make faculty time even more scarce. In Australia and Germany, CME requirements are expressed in terms of points to be accrued.

Without question, simulation-based training is more costly than exhorting learners to read or putting them in a room with a lecturer. But when regarding credits for continuous medical education (CME), reading a short article and answering a handful of questions can only generate 1 hour of credit—or as in Australia and Germany only a small amount of CME points, as can sitting through a lecture. Simulation training is generally much more interactive and much more intensive than other activities and therefore professionals earn more credits or points, which may make simulation-based CME financially competitive relative to simpler methods.

Simulation-based training allows a host of issues to be addressed that cannot be easily tackled in other ways. It is the belief of the authors—one that has been borne out by programs “voting with their feet” since the 1990s—that if simulator-based training is deemed to be desirable, innovative changes in the organization will evolve to allow it to occur.

But other emerging aspects also make patient simulation a beneficial tool for addressing future organizations’ needs. At the Harvard University hospitals, for example, the captive insurer, Harvard Risk Management Foundation, has taken unprecedented steps to link simulation-based continuous medical education training to discounts for medical malpractice premium rates for experienced clinicians in anesthesia and in obstetrics (J. Cooper, personal communication, 2005). This forward-thinking program is now being adopted by other malpractice carriers. In some jurisdictions, risk managers have chosen to invest directly in simulation activities at their institution, rather than to use the premium discount approach.

## COST OF SIMULATION CENTERS

The cost varies greatly depending on the scope of the facility and its programs, the nature of the target populations, and the extent of use by the different possible stakeholder groups. How the costs are allocated to different elements of an institution or consortium is equally complicated and depends highly on local conditions. No one formula for success exists. In some models, the center is wholly responsible for its own costs but is completely free to generate and retain revenue. At the other extreme is a model whereby the host institution bears all costs of operating a central core facility, but it collects any and all revenues and may even tax components of the institution (e.g., departments) to offset the costs. Perhaps most common are mixed models in which the central authority bears the costs of initial construction and outfitting (often funded by philanthropy) and some portion of the ongoing infrastructure (simulation

operations personnel, capital refurbishment, utilities), and each user (e.g., department) is responsible for providing instructors and paying for the marginal costs of any specific course or application. To date, few, if any, centers truly generate a profit, but many sites have successfully garnered external funds to offset some of the costs of training their own key target populations.

## Using Simulation for Assessment of Clinical Performance

Although the dominant use of simulation is for education and training, the first simulators (both Sim One<sup>175</sup> and CASE<sup>177</sup>) were created to be research tools to assess and understand the performance of clinicians. Such assessment could address routine work in clinical environments<sup>115,134,136,346,347</sup> as well as performance when responding to critical events.<sup>64,68</sup>

Note: the terms “assessment” and “evaluation” are often used interchangeably even though they have slightly different meanings, so the authors chose to do so in this chapter, too.

For further information on the assessment of clinical performance that is related to the topics of human performance and patient safety the reader is referred to [Chapter 6](#), where less simulation-related aspects of this topic are covered in more detail.

Performance can be divided into two components: (a) medical or technical performance, which is the appropriateness and thoroughness of the medical and technical response to the critical event; and (b) behavioral or non-technical<sup>348</sup> performance, which is the appropriate use of sound crisis management behaviors (e.g., leadership, communication, distribution of workload, decision making, etc.)<sup>24,349</sup> (see [Chapter 6](#)).

There are a number of potential frameworks that can be referenced when defining clinical and nonclinical competencies for the performance assessment of health care professionals. In different countries, different frameworks are used to describe anesthesiologist’s competencies, which provide the ground for assessment measures. Many countries build on the CanMed roles<sup>350</sup> (Canadian Medical Education Directives for Specialists) that describe seven roles for the competent physicians. Those roles are: medical expert, communicator, collaborator, leader/manager, health advocate, scholar, and professional. Other countries build on the six ACGME (Accreditation Council for Graduate Medical Education) core competencies, which include patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and systems-based practice.<sup>102</sup>

Assessment of medical, technical, and non-technical responses in simulation settings has resulted in a variety of tools for assessment and evaluation as suggested by different authors.<sup>64,69,89-93,97,99,101,136,342,349,351-354</sup>

For assessing the non-technical skills of anesthesiologists many investigators use the *Anesthesia Non-Technical Skills* (ANTS) system.<sup>91,353</sup> In recent years, the early ANTS evaluation system was adapted to different countries, and modified for different cultures<sup>351</sup> and health care specialties.<sup>355</sup> However, there are other tools for measuring

non-technical skills of anesthesia professionals. Of particular note is a rubric developed by Weinger, Gaba, and colleagues<sup>64,356</sup> which is simpler than ANTS but of equivalent capability.

## BENEFITS OF SIMULATION-BASED PERFORMANCE ASSESSMENT

Because the nature and cause of a simulated critical incident is known, one can construct in advance a list of appropriate technical activities.<sup>357</sup> Relative weighting of the importance of the different activities can be applied to reflect the fact that different activities, even if appropriate, differ in their importance. This weighting can be done either in advance of data collection, or post hoc (but in an appropriately blinded fashion). For example, when assessing medical or technical performance in managing malignant hyperthermia, termination of the trigger agent and administration of intravenous dantrolene would be highly important, indeed essential, items. Cooling measures, hyperventilation, and bicarbonate therapy would be among many appropriate (but less critical) responses. One can predict in advance specific technical errors to look out for. For example, for malignant hyperthermia management, these could include diluting dantrolene with the wrong diluent or an insufficient quantity of diluent.

Can the clinical outcome of a simulation predict how a real patient would have fared given the same care, and can this outcome be used in assessment? When watching a simulation scenario play out it seems tempting to think that the outcome of the patient—whether calculated by an underlying mathematical model of physiology (for a few simulators) or based on apparent adherence to patient care guidelines—can be the primary determinant of an individual assessment or a definitive prediction of what outcome a real patient would have had. Such a temptation is largely dangerous. Perhaps at the extremes of what transpired the apparent outcome could be reliable. If a patient is portrayed in ventricular fibrillation and nothing is done it is certain that they will die. If a healthy patient with substantial neuromuscular blockade receiving a FiO<sub>2</sub> of 50% oxygen is suddenly not ventilated for 30 seconds it is nearly certain that they will be fine. In between such extremes the exact outcome is very hard to predict. There will be isolated situations in which a mathematical model can predict certain physiologic variables, but the influence of those on other variables may be unknown. Why do some patients suffer an arrhythmia if their blood pressure falls below, say, systolic pressure of 50, 60, or 70 torr for a certain amount of time whereas others tolerate it fine? Why does one patient have return of spontaneous circulation after electric countershock applied at the same interval after dysrhythmia onset and another does not? Perfect decision making in resuscitation of a real patient cannot guarantee that electric countershock would successfully restore a normal cardiac rhythm. For the foreseeable future, any credible performance measurement technique must involve subjective judgments by clinical experts about the care process rather than about the calculated or presumed outcome.

## PITFALLS OF SIMULATION-BASED PERFORMANCE ASSESSMENT

**Technical versus nontechnical (CRM) skills.** As indicated in previous sections, it is feasible (if difficult) to assess a technical response to specific events and generic nontechnical behaviors (CRM). For which kinds of assessments is it appropriate to measure only technical performance, only nontechnical performance, or some combination of the two?

**Number of scenarios.** How many different scenarios are needed to achieve robust performance assessment of individuals in all relevant aspects (technical and nontechnical) of patient care? The literature suggests that the variability of individual performance across different scenarios is high, in fact greater than the variability across raters. If simulation is to be used to assess an individual a large number of scenarios would need to be conducted for each person. Having a larger number of scenarios is more effective in improving the reliability of ratings than is having a larger number of raters.<sup>64,237,358</sup>

**Rating individuals versus rating crews or teams.** Anesthesiologists work as individuals and in crews and teams with other anesthesiologists and with surgeons, nurses, technicians, and others. Should the performance of individuals working alone be assessed? Should anesthesiologists be able to call for and use help in solving problems? If so, can one still rate the individual when working with a team?

**Performance fluctuation.** How can performance that fluctuates substantially over time (i.e., during a simulation scenario) be aggregated into a single rating? This issue was recognized by Gaba and colleagues as a major apparent source of interrater disagreement.<sup>349</sup> It is not addressed by any current rating system.<sup>91,359</sup> One option is to conduct moment-by-moment rating to yield a high-resolution time series of the varying performance. A variety of mathematical techniques could then be applied to the time series to yield appropriate measures of aggregate performance and variation.

**Criterion thresholds.** What level of performance should be set as criterion thresholds for different purposes? Can benchmarks of performance be established by truly expert clinicians (recognizing that years of experience and hierarchic rank are not surrogates for expertise or skill)? Similarly, how does the rating system deal with single actions or behaviors that were lethal or harmful in the presence of otherwise good performance? If used for formative assessment, a rating system should indicate the successes of the examinee and the failures. If used for summative or high-stakes assessment, however, it may be critical to ensure that the examinee who risks harming a simulated patient cannot outscore another examinee whose overall performance is less strong but who at least did not endanger the patient. Not performing chest compressions in a cardiac arrest situation would be such a criterion for exclusion.

**Appropriate statistical analysis of validity, interrater reliability, and reproducibility of these assessments.** Various statistical tests and approaches have been used to evaluate these characteristics. The data on performance show various levels of interrater variance and high inter-

individual (and inter-team) variability.<sup>68,69,181,342,349,360</sup> As detailed by Gaba and colleagues,<sup>349</sup> some interrater reliability statistics are more stringent than others, especially in terms of the nature of the “by chance” benchmark. No firm consensus has been reached regarding which tests are most appropriate to answer key questions about simulation-based performance assessment. Some of the rating systems (including ANTS) have used less stringent tests of interrater reliability. Generalizability theory<sup>361</sup> offers a set of statistical techniques to sort out the impact of scenario, subject, rater, number of scenarios, and other facets on such assessments. This technique specifies how comparisons can be made against reference performance levels or as relative comparisons between subjects without a fixed benchmark.

Although simulation should provide a useful window on performance assessment, it remains challenging to develop widely accepted performance measures of anesthesiologists’ skills,<sup>362</sup> even if the simulator is used as a tool to present standardized scenarios.<sup>363</sup> Klemola and Norros<sup>364</sup> published a newer way of looking at performance that involves anesthesiologists’ habit of actions. These authors distinguished between reactive habits (conservative, self-contained, reluctant to construct subjective evaluations) and interpretative habits (creative, interactive, continuous integrative reasoning). They showed that many issues must be considered when discussing the best method of education and evaluation. Additional issues include defining and assessing professional competence.

## USING SIMULATION FOR THE EVALUATION AND TESTING OF ANESTHESIA PROFESSIONALS

The use of simulation as a tool for performance assessment has presumed advantages: scenarios are known, errors can be allowed to occur and play out, and intensive recording and archiving of performance is possible. Simulation provides a unique window on performance that is prospective and about challenging situations, whereas routine observation of real work is prospective but most commonly only sees less challenging situations, and case reports about performance may be of tough cases but are often incomplete and hindsight-based.<sup>365</sup> Scoring or certifying competence by using the simulator is more problematic than using the simulator as a teaching tool, however. Anesthesiologists have long discussed the possibility of using the simulator as a tool for examinations, either for graduation from a residency or for ABA certification. In Israel, a simulation examination has become part of the board certification process.<sup>95</sup>

Despite these difficulties, the use of anesthesia simulation to assist in evaluating performance is likely to increase in the future. Even though simulation is currently used for some high-stakes examinations, the challenges remain the same: (1) It requires independent evaluation of the simulation scenarios and assessment of the predictive power of the subjective judgments made by experts scoring the examinee. (2) There is a lack of any well-accepted standard for performance evaluation.

Another difficulty with using simulation for high-stakes testing at a neutral site is that the operating room equipment would rarely be the same as that used by the candidate, and

the operating room staff’s operational protocols could differ from the protocols familiar to the candidate. In the training situation, these difficulties can be overlooked as part of the global suspension of disbelief needed to maximize the benefits of simulation training. In the test situation, these differences potentially could skew the results. This issue could be addressed by allowing candidates preparing to take their examination to undergo sufficient practice sessions to familiarize themselves fully with the standard simulation environment used for the test.

Another application of simulation-based performance assessment would be for the evaluation of trainees or experienced clinicians who have been placed on probation or for whom dismissal from their position is already a distinct possibility. For these clinicians, the burden of proof is on them to show their skills. Simulation could offer a more controlled environment for these clinicians to do so. The same could be true for practitioners who wish to return to clinical work after a hiatus.

The existing systems of performance evaluation, which use a haphazard composite of subjective judgment of clinical competency in clinical work along with written and oral examinations, has itself never been validated. Many experts believe that the written examination does not correlate well with clinical ability, and the degree to which the oral examination process tests actual clinical skill is unknown. Simulation could offer candidates the opportunity to show their clinical abilities in a controlled clinical domain; appropriate scenarios can probe language skills and the ability to act as an effective consultant to other clinicians.<sup>226,366</sup>

The ABA transitioned in 2017 to a new format for the Part 2 Examination, named the APPLIED Examination, to include an Objective Standardized Clinical Examination (OSCE) component along with the traditional structured oral examination component. The OSCE stations do not include full-scale mannequin-based simulation but do include performance on task trainers and encounters with actors playing roles as patients or as clinical personnel (e.g., surgeon).

The methods currently used to assess the performance of clinicians in their actual clinical work are weak and inconsistent; systematically incompetent anesthesia professionals are not easily identified or removed from practice. Thus, reasonable arguments can be made that the field of performance assessment has advanced sufficiently to allow consideration of simulation-based examinations, including full mannequin-based simulations, even for high-stakes purposes, especially considering the limitations of the current systems of written and oral examination.<sup>366</sup> Nonetheless, simulation-based performance assessment remains a controversial topic for discussion in the simulation and clinical anesthesiology communities. The anesthesia professions should be careful about how they may introduce simulation-based performance evaluation. The controversy should not divert attention from the most common application of simulation, which is to improve clinical performance through training individuals and teams to prevent and manage adverse clinical events.

## Simulation Societies and Simulation Journals

One measure of the evolving maturity of simulation in health care is the formation and growth of professional

societies and associated peer-reviewed journals. Organizations such as the Society for Simulation in Health Care (SSH) and the SESAM ([www.sesam-web.org](http://www.sesam-web.org)) have been constantly striving to promote knowledge and use of simulation in health care. Although anesthesiology was the medical field that initiated work on the fully interactive mannequin-based simulator and that dominated the early developments in the field, simulation is a broad strategy that has now been widely adopted by many different disciplines and domains in health. For the most part, simulation professional societies have sprung up as explicitly multidisciplinary organizations, while clinical societies have also created committees and other bodies to oversee or facilitate the use of simulation in their settings. Major leadership roles in the multidisciplinary societies have been played by anesthesiologists and engineers associated with anesthesiology far more frequently than their prevalence in the clinician population would otherwise predict.

Periodic scientific congresses on simulation such as the Rochester Conferences on Simulation in Anesthesia have been under way since the mid-1990s although attendance was less than 100 people. The largest simulation organization is SSH, which was founded in 2004 as the outgrowth of the group that had operated the International Meeting on Medical Simulation for several years as a satellite to the annual meeting of the Society for Technology in Anesthesia. Under the auspices of SSH, the meeting was transformed into the IMSH, encompassing all health care disciplines and domains, not just medicine. Although starting with far fewer attendees, the annual meeting of SESAM now has around 850 attendees (2018). Similarly, for SSH, whereas the original IMMS had at most 200 attendees, IMSH in 2018 had more than 3000 attendees. For IMSH this number places it in the category of a medium-sized scientific meeting; to put this in the context of anesthesiology, it would rank as the third largest meeting in the United States, falling below only the ASA meeting (about 14,000 attendees) and the New York Postgraduate Assembly in Anesthesiology (PGA) conference (over 4000 attendees), but ranking ahead of the International Anesthesia Research Society (IARS) annual meeting (about 1000 attendees).

Another sign of the growing maturity of simulation in health care is the establishment and growth of peer-reviewed journals for the field. SSH has published *Simulation in Healthcare* in print and online every other month since 2006. This journal was approved for indexing by PubMed in 2008. Many organizations have become affiliates of SSH and most have made *Simulation in Healthcare* their official publication (for example the Australian SSH, and the Association of Standardized Patient Educators). The International Nursing Association for Clinical Simulation and Learning has published (online only) the *Journal of Clinical Simulation in Nursing* since 2006 although it rarely has papers concerning anesthesiology. The BMJ *Simulation and Technology-Enhanced Learning*, the journal of the UK Association for Simulated Practice in Healthcare, has been published (online only) since 2014. *Advances in Simulation*, the official journal of SESAM, has been published (online only) since 2016.

## The Future of Patient Simulation in Anesthesia

*The future is now—we are it.*<sup>234</sup>

More than three decades of consistent development have passed; the field of simulation in health care could be described metaphorically as being in its adolescence or young adulthood. Thousands of simulators are in use around the world in thousands of clinical programs. Anesthesiology and critical care remain important mainstays in simulation, which is now a standard part of the training of anesthesia professionals, although these fields have now become minority users when compared to numerous users across all the rest of health care. Yet even in anesthesiology, with nearly 30 years of simulation under its belt, the fraction of anesthesia professionals who have undergone a serious simulation experience since completing their initial training is relatively small. For example, as of 2018 Gaba estimates that only about 25% of board-certified anesthesiologists in the United States have undergone the MOCA simulation course.

The modalities of simulation have expanded from completely nontechnological to fully virtual. MBS have become more sophisticated, easier to use, and more portable, and available in many different models from multiple manufacturers. On the other hand, considering that it is now nearly 25 years since the first commercial simulators were introduced, the overall improvement in the features, reliability, and clinical or physical realism has not advanced at nearly the rate as for computing equipment over the same period. In part this is due to the fact that improvements in simulators depend heavily on the demand for the devices in general, and for special features in particular. There is a steep tradeoff between features and many otherwise desirable improvements may be too costly for their expected impact or demand. Simulators that use complex mathematical models of physiology and pharmacology have largely retreated from the marketplace since many applications can be managed well with less complicated control systems.

In contrast to aeronautical engineers designing airplanes, anesthesia professionals or biomedical engineers do not design and build human beings. In aviation the fundamental differential equations of fluid mechanics and aerodynamics are firmly established, allowing supercomputers to provide technically meaningful simulations as replacements for many physical tests; furthermore, test flights of prototype aircraft are conducted with sophisticated instrumentation built in to test and carefully capture their behavior. Clinicians will never have this type of knowledge about the human body.

VR and AR are still in an early childhood phase, with rapid development under way but with maturity still far away. Many current (late 2018) VR systems address visualization of anatomy or physical structures. Only a few provide multiparicipant interaction in an immersive virtual environment. As far as the virtual patient is concerned they are only as good as the underlying engines—mathematical or otherwise—that drive their clinical responses. The coming decade(s) will likely see a continued proliferation of VR systems with substantial shakeout of techniques, technologies, and firms. Currently many users of simulation are beginning to try out VR and AR systems but it is still very early in their development and use.

VR proponents imagine a VR so realistic that it rivals, or is indistinguishable from, the real world. This would approach the *Star Trek* holodeck or the “brain in a vat” style of simulation in *The Matrix*. Although we once predicted that interactive VR could take over from physical simulation by 2020 to 2025, and the tide has indeed started to turn, we predict that it will still be a long time—if ever—before this happens. Whether there is indeed something fundamentally different about human professionals working together naturally in a physically realistic clinical environment versus doing the same via some sort of VR remains to be seen.

Patient simulation has now become a regular part of initial and recurrent training of most anesthesia professionals and many other clinicians in many countries in the developed world, and significant penetration into the developing world. Zero to low technology simulations are also being used successfully in low resource areas to address important health issues.

With patient simulation issues of human factors and patient safety, in part via the CRM concept, were introduced to health care as ACRM training and its equivalents in various clinical arenas. This has been an influential complement to traditional methods and content of teaching and learning in a large variety of health care domains, especially those that share the complex and dynamic work profile of anesthesiology—decision making playing out over seconds, minutes, and hours; working with action teams; wielding highly lethal interventions as described in [Chapter 6](#). Since all of the pioneering work on mannequin-based simulation and its key applications was done in anesthesiology, our field can rightly claim to have given one more gift to all of health care, to accompany other gifts such as the Apgar score, modern pulse oximetry and capnography, blood gas analysis, mechanical ventilation, etc. Moreover, despite its wide spread beyond anesthesiology, anesthesia professionals and others working with them continue to play major leadership roles in multidisciplinary and multiprofessional simulation centers and organizations.

Fully integrated simulation team training with a significant focus on human factors and CRM may improve patient safety and quality in acute care settings, and it may increase employee satisfaction and effectiveness of routine work. Simulation team training is becoming more common, but is still not solidly embedded into the fabric of health care as a core part of how we do business as is the case for commercial aviation or nuclear power. While health care has a long way to go to achieve the full impact of simulation on the quality and safety of patient care, the authors no longer fear that the technique of simulation will be rejected in our field, and they believe it is worth it to remain on a path toward the comprehensive industrywide, career-long application of simulation to save as many hearts, brains, and lives as possible.

## Appendix 7.1 Online Links and Useful Resources

- American Society of Anesthesiologists (ASA) Simulation Education Network
  - Many resources on simulation and links to ASA-endorsed simulation centers
- Society for Simulation in Healthcare (SSH)
  - Homepage: [www.ssih.org](http://www.ssih.org)
- Journal *Simulation in Healthcare*, Elsevier: <https://journals.lww.com/simulationinhealthcare/pages/default.aspx>
- Website of the Instructor Certification program of SSH: <https://www.ssih.org/Certification>
- Criteria for Accreditation of Simulation Centers by SSH: <https://www.ssih.org/Accreditation>
- Society in Europe for Simulation in Medicine (SESAM): [www.sesam-web.org](http://www.sesam-web.org)
- Stanford Simulation Site - *Center for Immersive and Simulation-based Learning*: [cisl.stanford.edu](http://cisl.stanford.edu)
- Center for Advanced Pediatric and Perinatal Education (CAPE): [cape.stanford.edu](http://cape.stanford.edu)
- Center for Medical Simulation (CMS in Boston): [harvardmedsim.org](http://harvardmedsim.org)
- WISER Simulation Center—University of Pittsburgh Medical Center: [www.wiser.pitt.edu](http://www.wiser.pitt.edu)

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## KEY POINTS

- Deontologic ("rules-based") ethical theory and utilitarian (outcome-based) theory clash in clinical scenarios in which the interests of individual patients are pitted against the interests of larger populations.
- In the United States, the predominant medical ethical principle is that of respect for the patient's autonomy, and its expression is in the informed consent of patients for medical therapy.
- Competent and autonomous individuals can make affirmative choices about their medical care and refuse any medical treatments, including lifesaving care. Competence is both functional and relative. Four elements of competent decision making are understanding, appreciation, reasoning, and evidence of a choice.
- Minor patients have varying degrees of decision-making capacity, and they may have legal rights to make certain decisions. Pediatric patients should be involved to the degree that they can be in medical decision making, particularly regarding elective therapy.
- Medical testing should follow the ethical principles of beneficence and nonmaleficence and should be based on clinically validated algorithms whenever possible. Medical tests with special social significance, such as pregnancy and human immunodeficiency virus testing, should be undertaken only with the patient's informed consent and should not be undertaken without sound evidence that they are necessary and beneficial.
- In general, the rights of pregnant women are weighed against the rights of fetuses in a decremental fashion as the fetus approaches and surpasses viable age. Laboring women are able to give informed consent, and the validity of "Ulysses directives" at the time of labor is ethically arguable.
- Use of restraints is antithetical to promotion of autonomy, and anesthesiologists have both ethical and legal obligations to determine whether such extreme intervention is warranted. Coercing or using physical or chemical means to force competent patients to undergo treatment they are refusing is both unethical and illegal.
- Respect for patients' autonomy requires that we disclose mistakes to release patients from misconceptions about their medical past and enhance their ability to share decision making about their medical care.
- An advance directive is a document executed by the patient before incapacity to provide the patient's physicians with guidance in medical decision making when the patient cannot communicate for himself or herself: these directives include, but are not limited to, durable powers of attorney, living wills, transfusion decisions, do-not-attempt-resuscitation (DNAR) directives, and decisions regarding organ donation.
- Surrogate decision makers explicitly act in "substituted judgment" to provide what the patient would have wanted and are not being asked merely for their own preferences. Surrogate decision makers at best only approximate the patient's decisions.
- Patients have moral and legal rights to refuse even life-sustaining therapy, including in the operating room. DNAR orders should not be automatically suspended for anesthesia and/or surgery, but rather require reconsideration of risks and benefits; the goals and decisions of competent patients should generally be honored.
- Terminal care requires special knowledge and experience on the part of the physician. It requires expertise in medically supportive therapy, management of problematic symptoms, knowledge about physiologic changes in the dying patient, support and counseling of patients and families, understanding and respect for the patient's autonomy and religious and cultural practices and beliefs, the ability to work within complex healthcare teams, the ability to communicate well, and empathy.
- Several interventions have special ethical implications—fluid and nutritional management; the administration of sedatives and/or narcotics that have the potential to hasten death; the institution of deep continuous sedation; the administration of neuromuscular blocking agents; and deactivating pacemakers, ventricular assist devices, and implanted cardioverter-defibrillators.

- Physician-assisted suicide (PAS) is the provision of medication and/or prescriptions to patients at their request for the purpose of ending their life. Euthanasia is the administration of medication by someone other than the patient for the express purpose of causing death. PAS and euthanasia are legal only in specific parts of the world, but they are strongly supported by the public.
- Brain death is legally and medically defined as the point at which all cardiorespiratory function irreversibly ceases or all function of the whole brain irreversibly stops.
- In donation after cardiac death (DCD), withdrawal of life support occurs with provisions for immediate organ donation after cardiac arrest. Controversies around DCD include concerns about when cardiopulmonary death can be declared and whether medications that preserve organ function but may hasten the donor's death can be administered.
- Research in human subjects must balance many conflicting interests such as the needs and rights of the research subject; the hypothetic interests of future patients; and the physician's financial, professional, and personal goals. The ethical conduct of research in human subjects follows three principles: (1) respect for autonomy, and the obligation to protect subjects with limited autonomy; (2) beneficence, with obligations to minimize risks, maximize benefits, and ensure that the research design is scientifically sound; and (3) justice, the obligation to treat each person with regard to what is morally right and to ensure fair distribution of benefits and burdens.
- Advances in understanding animal cognition have led most biologists to believe that many, if not all, animals are capable of feeling pleasure, pain, anticipation, and fear, and thus they experience both enjoyment and suffering. Allowing animal suffering because of pain, fear, sickness, or poor standards of care is a moral harm that must be avoided, mitigated, and weighed heavily against the benefits it produces.
- U.S. professional organizations for physicians have consistently stated that participation in executions by physicians is unethical, and the American Board of Anesthesiologists states that participation in executions would constitute unprofessional behavior that would result in investigation and possible decertification of anesthesiologists.
- "Conscientious objection" by physician to providing legally allowable medical care that violates their personal moral values is possible, but is limited and counterbalanced by a physician's professional obligations to put the patient's interests first.

Medicine is a respected profession with codes of behavior and definite rules of conduct. Modern medical practitioners have tremendous power, recognized social import, and powerful financial interactions that touch nearly everyone's lives. The American Society of Anesthesiologists (ASA) has established principles for the ethical management of patients.<sup>1</sup> This chapter examines the ethical bases of the practices of medicine and the implications for anesthesiologists.

## Ethical Theory

### VIRTUE ETHICS, UTILITARIANISM, AND DUTY-DRIVEN ETHICS

The classic "paternalism" of medical practice was derived from *virtue-based ethics*. In this view, the physician is a genuinely virtuous person with inherent qualities of competence, sincerity, confidentiality, and altruism, who naturally knows and does what is correct for the patient. The patient, uneducated about medicine, has to trust the physician to decide what is best. Western society and legal systems have changed substantially since paternalism flourished, giving way to practices based in the four "pillars" of medical ethics: respect for patient autonomy, beneficence, nonmaleficence, and justice. Many different ethical frameworks are applied in modern medicine, but two of the most prominent frameworks relevant to western medicine are utilitarian ethics and deontology.<sup>2</sup>

In *utilitarian ethics*, actions are judged right or wrong on the balance of their good and bad consequences. A "right" action produces the most good, based on a perspective that

gives equal weight to the interests of all affected parties. Utilitarian theory is compelling but falls short in defining which benefits are most important. Is it the "good" that all reasonable people want or the "good" defined by the individual patient? What if the only way to maximize good is to commit an entirely immoral act? For example, what if the only way to win a war is to systematically torture children? Outcomes of actions continue to accumulate over time—when on that continuum is it appropriate to determine that an action was right or wrong? The "good" act of saving an individual's life today may be viewed through a completely different lens when, 20 years from now, that same individual is revealed as a mass murderer.

Utilitarian theory may be best when applied to analyzing broad-based policies, in decisions regarding rationing of resources, and when attempting to resolve conflicting ethical obligations between several equally interested parties.

The premise of Kantian-based ethics (also called deontologic—or *duty-based*—theory) is that features of actions other than their consequences make them right or wrong. *Intention* is more important than outcome. Furthermore, no person should use another exclusively as a means to an end, because each person is the end for which we should act. No person should be used to further the purposes of another person without that other person's autonomous consent. Kantian philosophy would forbid killing one innocent person to save another innocent person, for example.

Individualism and autonomy are valued highly in Western society, and people tend to turn to Kantian philosophy when ethical questions arise that balance the authority of the physician against the goals and values of individual patients.

Some of the toughest ethical questions in medical practice occur when the rights and desires of individual patients conflict with social policies. Clashes between deontologic and utilitarian principles are common in the intensive care unit (ICU), in managed care settings, in end-of-life care, in transplant medicine, in triage during civilian mass casualty events, and in the care of poor and older patients whose medical management is funded by the government. In each of these settings, the will of the individual patient may conflict with broader principles of minimizing expense, fairly allocating scarce resources, protecting the broader interests of many patients, and determining where and how society's healthcare dollars are best spent.

The political tradition of the United States provides a clear underpinning to individual freedom, and at the beginning of the 20th century, the concept of the autonomy of patients began to emerge.

## Clinical Ethics

### INFORMED CONSENT AND INFORMED REFUSAL

Legal and moral imperatives for informed consent are based on the ethical principle of respect for patient autonomy. *Autonomy* refers to the ability to choose without controlling interferences by others and without personal limitations that prevent meaningful choices, such as inadequate information or understanding.<sup>2</sup> Individuals have the right to determine what happens to them to the degree to which they are capable. In the United States, this right is rooted in constitutional guarantees of privacy and noninterference.<sup>3</sup> In 1914, the case of *Schloendorff v Society of New York Hospital* established that it was the right of "every human being of adult years and sound mind to determine what shall happen to his own body."<sup>4</sup> In 1957, the term *informed consent* was first used in the case of *Salgo v Trustees of Leland Stanford Hospital*, which established that it is not sufficient for physicians simply to secure consent; physicians have a duty to inform patients about the risks and alternatives to treatment, in addition to the procedures themselves and their consequences.<sup>5</sup>

Respect for the patient's autonomy requires physicians to respect decisions made by competent patients, but also to *promote autonomy* by removing barriers to competent participation in decisions. Such obstacles range from incomplete or inaccurate information to reversible medical conditions that impair a patient's ability to understand the information given to him or her.

### Competence and Capacity

Autonomy to make medical decisions cannot exist in the absence of competence. In the United States, *competence* is a legal determination, and *capacity* describes the necessary skills to participate in medical decisions. Most often, the terms are used interchangeably.<sup>3</sup>

Impairments of capacity can be temporary or permanent. Examples include some mental illnesses, dementia, immaturity, anxiety, and pain. Medication effects can variously impede competence, or improve it, depending on their effects and the context in which they are given. Older patients, patients suffering from mental impairment, and children are

particularly vulnerable to having their participation in medical decisions inappropriately curtailed or denied because their capacity to participate is frequently underestimated. Hearing loss, expressive aphasia, and other neurologic impairments can create the false impression that capacity is impaired. Many minors have the ability to make medical decisions but may be mistakenly excluded from the decision-making process solely because of their age. Language barriers can present significant challenges to communication.

Capacity is both relative and task specific. Patients may be able to understand and make decisions about medical issues while being unable to manage their financial affairs, for example.

Prejudice and paternalism permeate physician behavior in the informed consent process. Challenges to a patient's competence frequently occur because the patient and the physician have a difference of opinion or values,<sup>3,6,7</sup> and the majority of referred patients are found competent.<sup>3</sup> Unwarranted challenges of a patient's capacity may, intentionally or not, serve to allow the physician to dismiss, rather than solve, a dilemma regarding a difficult patient's wishes, since with a finding of incapacity, the physician's paternalism cannot then be trumped by patient autonomy. In a retrospective study, Katz and associates commented that referrals for urgent or serious treatment put pressure on a consulting psychiatrist to support the medical team's wishes for intervention by simply declaring the patient incompetent.<sup>8</sup> Treatment refusal may simply reflect a patient's prioritization of other things (e.g., dignity, privacy, independence) other than medical outcomes, and not a problem with capacity—or it might reflect manageable emotions and values that disproportionately affect a patient's choices, but do not necessarily rule out capacity.

Doctors are mistaken about patients' preferences regarding life-extending therapies and underestimate older patients' desires for life-extending therapies in 30% to 40% of cases.<sup>9,10</sup> Moreover, surveys indicate that physicians and other healthcare workers are likely to *act* on their personal prejudices regarding handicapped or impaired patients.<sup>11</sup>

Functional capacity for decision making must be judged separately from the perceived quality of the decision itself. Patients have the right to make "bad" decisions (i.e., decisions that *the physician* feels are less than optimal) if they are competent and have appropriate information.<sup>7</sup> Otherwise, the physician would merely prevail whenever a disagreement occurred, and patient autonomy in medical decision making would be nonexistent.

How do we recognize competence? Competence is defined *functionally*, and it is *task specific*.<sup>2</sup> It cannot be defined to be absent by the mere presence of specific diagnoses or medications.<sup>12</sup> Furthermore, evidence of *impairment* is not sufficient to prove *incompetency*. With such high value placed in the United States on autonomy and self-determination, incompetency is, and should be, a difficult bar to leap over, requiring that only persons with impairments "that place them at the very bottom of the performance curve" should be declared incompetent.<sup>12</sup> A "sliding scale" approach to competence determinations, rather than an all-or-none approach, is endorsed by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research,<sup>13</sup> and generally reflects how courts deal with competency cases.<sup>12</sup>

Anesthesiologists frequently ask whether valid consent can be obtained after the patient has received premedication. Claims that premedications automatically invalidate consent demonstrate a lack of understanding of the concept of competence. If it were true that benzodiazepines and narcotics, for example, automatically invalidate consent, then we would have to consider the consent of almost all chronic pain patients invalid. In one study, 37.5% of geriatric patients presented for surgery having taken self-prescribed medications and over 25% of these were analgesics and benzodiazepines.<sup>14</sup> If competence were automatically invalidated by the presence of specific medications, then we would be forced to carry out drug testing on all preoperative patients before obtaining consent. While it is true that *sometimes* premedication can interfere with a patient's ability to give consent, in some circumstances, patients cannot give consent *without* premedication. A patient who is in severe pain, for example, is unlikely to be able to focus on detailed risks and alternatives of a proposed procedure without first receiving medication. In that case, treatment of severe pain may actually *improve* competence during the informed consent process.

How does the anesthesiologist determine if they are dealing with a competent patient? Multiple reviews by competency consultants agree that there are several functional elements to competence: (1) *Understanding* - Can the patient receive and understand treatment-related information? (2) *Appreciation* - Does the patient have insight about the disorder and its consequences and potential treatment options? Does the patient understand that treatment could be beneficial in some way? (3) *Reasoning* - Is the patient able to use logic to compare the risks and benefits of treatment alternatives? And, (4) *Evidence of a choice* - Can the patient communicate a choice?<sup>3,12,15</sup>

In respecting and promoting patient autonomy in medical decision making, the anesthesiologist has an ethical duty to treat reversible conditions that interfere with medical decision making when doing so would not delay the medical treatment so much that it becomes irrelevant. Elective surgery may have to be postponed until expert consultation for a determination of mental capacity or treatment of reversible conditions can occur. When surgery in an impaired patient is urgent, the anesthesiologist may have to rely on a surrogate decision maker or proceed with the best determination of the patient's interests in mind. It is important to note that the mere presence of an emergency does not invalidate a *competent* patient's rights to consent to or to refuse treatment. Overriding a competent patient's wishes is unethical, even in emergency situations.<sup>16</sup>

## Disclosure

The informed consent process requires honest disclosure of medical information to the patient. U.S. courts generally rely on two standards of disclosure, termed the reasonable person (or objective person) standard and the subjective standard. In the reasonable person standard, the physician must disclose any information that a theoretically reasonable person would want to know, and the risks or cluster of risks to which a reasonable person in the patient's position would attach significance in deciding whether or not to forgo the proposed therapy.<sup>17,18</sup> This standard does not require an exhaustive recitation of facts, and it acknowledges that

not all information related to the procedure is integral to making a decision about whether to undergo that procedure. The subjective standard recognizes that some patients may have special needs for specific information, and when that need is obvious or has been brought to the attention of the physician, the information must be disclosed. A concert violinist may have a specific need to know about the potential for nerve damage from an axillary block, while an opera singer may need to know that intubation may adversely affect the voice. In obtaining informed consent, the anesthesiologist should always ask the patient if there are any special concerns regarding the anesthetic, or anything he or she would want the provider to know. In general, legal and ethical standards now require that the physician (1) accurately discuss the therapy and its potential alternative—including no therapy—and (2) disclose the common risks, because they are more likely to happen, and the serious risks, because the consequences are severe.

The doctrine of *therapeutic privilege* is sometimes cited to avoid discussing risks, the reasoning being that discussing risks can psychologically or physically harm the patient by increasing stress. Studies of patients' stress during the informed consent process *do not* support this concept. These studies show that patient stress is generally reduced after risk discussions<sup>19,20</sup> and omission of such conversations is contrary to U.S. law. Although it is ethical to forgo or curtail risk discussions at the patient's request, it is not ethical for the physician to decide to do so unilaterally.

The physician-patient relationship is inherently unequal because of the physician's knowledge and authority and the patient's dependence on the physician for care. Physicians have ethical obligations to avoid exploiting their influence for the purpose of accomplishing their own ends. Although offering a rational basis for a medical choice is acceptable, it is always unethical to coerce or manipulate competent patients into decisions by presenting real or implied threats or by omitting or misrepresenting key information. In fact, such intentional manipulations are morally equivalent to lying to the patient, and thus invalidate the concept of informed consent entirely.<sup>21</sup>

## Legal Implications of Informed Consent

The informed consent process does not prevent legal liability when adverse events occur. Flawed informed consent processes have been cited, however, as evidence of a lack of quality of care by the physician, and are associated with poorer litigation outcomes for the physician.<sup>22</sup> The ASA closed-claims database reveals that informed consent is cited in approximately 1% of cases, and cases with inadequate informed consent documentation are associated with larger monetary awards.<sup>23</sup> Studies show that the risk of a malpractice claim is directly related to the patient's perception of his or her relationship with the physician.<sup>24</sup> The informed consent process provides one of the few opportunities anesthesiologists have to establish that relationship, however brief, and the medicolegal importance of that process should not be underestimated.

## Informed Refusal

The concept of informed consent is moot if the informed patient cannot refuse medical therapy, because every informed consent process would then have to end with

the physician getting his or her way. Examples of informed refusals in anesthesiology include requests to withdraw or withhold life-supporting care in the ICU; do-not-attempt-resuscitation (DNAR) orders in the operating room; refusals of blood transfusions; and cases in which a patient refuses preoperative testing, such as human immunodeficiency virus (HIV) or pregnancy testing.

Informed refusal has concerns and requirements similar to those of informed consent. When patients refuse medical care or insist on what the physician believes to be suboptimal care, disclosure of the risks and benefits becomes even more important because these decisions may veer from options that are already widely accepted and for which the risks are believed to be lowest. It is easier to justify agreeing to the unusual preferences of a well-informed patient than to justify subjecting a poorly informed patient to unorthodox care.

Despite full information, patients may sometimes request or demand care that is unreasonable, either because it will adversely affect the performance of a surgical procedure or because it would be associated with unreasonably high risks. When a patient demands a technique that is inappropriate or outside of the realm of reasonable practice, the anesthesiologist is under no ethical obligation to provide that care. No physician can be compelled by a patient to practice negligently.

## Special Issues in Informed Consent and Informed Refusal

### THE JEHOVAH'S WITNESS PATIENT

The classic example of a patient who refuses therapy in anesthesia practice is that of Jehovah's Witnesses, many of whom believe that accepting a blood transfusion violates a Biblical injunction. The Jehovah's Witness doctrine has been subject to change over time, with resulting inconsistencies in religious practice regarding which, if any, blood components may be acceptable. Individuals interpret religious doctrines in light of their own spiritual contexts, and not all believers hold to the same tenets with identical fervor. Church doctrines, like medical practices, evolve over time, and practices that are acceptable at one time may not be years later. Anesthesiologists and surgeons have cited individual and doctrinal inconsistencies as justification for ignoring the wishes of Jehovah's Witness patients, but to do so is no more logical than assuming that every hypertensive patient needs or will respond well to identical treatment or that optimal treatments will not evolve over time. Moreover, *any* patient has the right to refuse blood transfusion therapy, regardless of whether this desire is founded in religious preference. Such refusals have become more common in patients who are not Jehovah's Witnesses, as blood transfusion therapy has been connected to infection risk and other complications.

Because of the differing beliefs of Jehovah's Witness patients, the anesthesiologist must have a thorough and detailed preoperative discussion of possible therapies with the patient, and the conclusions should be documented in the patient's chart. A physician who cannot comply with a competent adult patient's desire to forgo transfusion has an

ethical obligation to find an alternative caregiver whenever possible.<sup>25,26</sup>

The courts strongly support the rights of most adult patients to refuse blood products for themselves but have been inconsistent and have interfered in cases of some pregnant patients. Transfusion of pediatric Jehovah's Witness patients by court order is common. However, this may become ethically and legally less acceptable as alternative bloodless therapies to maintain oxygen-carrying capacity evolve, as the Jehovah's Witness church further defines its doctrines with regard to children, and as the capacity of children to consent to or refuse therapy is better understood.

### THE PEDIATRIC PATIENT AND OTHER PATIENTS WITH IMPAIRED COMPETENCE

The ethical practice of medicine weighs heavily toward adherence to the respect for autonomy of competent patients or advance directives of patients who were previously competent. Medical care of individuals who have never been autonomous relies on principles such as respect for human dignity, beneficence, avoidance of harm, and adherence to the principle of justice.

Children are examples of persons who may or may not yet be autonomous. Laws in each state define the age at which children become legally competent to make medical decisions (usually 18 years), but many younger children have the mental and emotional capacity to make medical decisions. Forcing such individuals to undergo treatments they do not want is unethical and could be illegal as well.

Decision-making capacity in children is variable. Most 2-year-old children are clearly not able to make medical decisions. However, the range of capability in children as young as 7 or 8 years old is wide. In one study, children 6 through 9 years of age who were invited to participate in influenza vaccine research asked pertinent questions about individual risks and benefits and whether their community and other children would benefit.<sup>27</sup> Studies suggest that the average 12-year-old adolescent has capabilities that are required in medical decision-making, but differing influences of the brain's well-developed reward system coupled with underdevelopment of the brain's control systems suggest that decision-making capacity may in fact be diminished in specific contexts in this age group.<sup>28</sup>

Most states recognize "emancipated minor" status, in which a court determines that a minor can legally make medical decisions for himself or herself. Legal exceptions to the age of consent are recognized in most states when treatment is believed to be in the minor's best interest and when a requirement for parental consent would interfere with the child's ability to receive medical help. The law recognizes that, tragically, some conditions for which a minor seeks therapy may even be the result of parental abuse and seeking parental permission for treatment may actually further endanger the minor. One quarter of pregnant teens are at risk for physical or sexual assault, and the most common perpetrator is a member of their family.<sup>29</sup> Thus, minors are allowed in many states to consent for treatment for substance abuse, sexually transmitted disease, mental illness, and medical care affecting pregnancy, including abortion, without seeking parental consent. When a minor has decision-making capacity but is not "emancipated," a judge

may declare the child to be a “mature minor” with decision-making rights.

Ideally, individuals of any age should be involved in medical decisions to the degree that their capacity allows. Children ages 7 to 17 have been shown to desire comprehensive perioperative information, including details of the procedure and anesthesia, risks, and complications.<sup>30</sup> A minor with capacity to make decisions should not be coerced or restrained under most circumstances.<sup>31</sup> Determining whether a minor has such capacity may require formal consultation and assessment. The American Academy of Pediatrics has stated that physicians who care for children “should give serious consideration to each patient’s developing capacities for participating in decision making, including rationality and autonomy.”<sup>32</sup> The term *assent* rather than *consent* is used to refer to agreement to treatment from children who do not fall into legal categories, such as age, that award adult rights. Recently, authors have suggested that informed *consent* rather than *assent* for medical research participation should be applied to children ages 12 and up.<sup>33</sup>

When children dissent from medical care, persistent refusals may be ethically binding, particularly in the case of participation in research. Medical personnel should respect the wishes of a patient who withholds assent and should try to gain a better understanding of the patient’s situation or deal with his or her fears. “A patient’s reluctance or refusal to assent should also carry considerable weight when the proposed intervention is not essential to his or her welfare and/or can be deferred without substantial risk.”<sup>32</sup>

### Ethical Challenges of Preoperative Testing

The ethical implications of genetic testing have been widely discussed in the literature, but the ethical implications of routine medical testing have been largely overlooked by professional societies. The performance of diagnostic tests does have ethical dimensions, however. We generally undertake such tests precisely because we intend to help the patient (beneficence) or to use the information to minimize other risks (nonmaleficence). Certain medical tests may also carry implications for the patient’s autonomy, privacy, and even social justice.

### ROUTINE PREOPERATIVE TESTING PROTOCOLS

Preoperative testing may help identify unrecognized or disguised conditions that could adversely affect anesthetic risk. All medical tests carry risks, however. False-positive and false-negative results may either label patients as having a condition they do not have or inappropriately assure patients that they do not have a condition that they do. Erroneous results may lead either to further testing or to inappropriate and unnecessary therapy associated with further complications. Errors can also cause patients to be deprived of important therapy they would otherwise receive. Tests sometimes have accompanying physical complications, and they are certainly always associated with economic costs. Systematic over-testing increases the costs of health care for entire populations, unnecessarily burdening an already costly system, and diverting badly needed funds to unnecessary enterprise. Medical tests may involve problems of conflicts of interest if the ordering physician has an

economic relationship with the entity that carries out the tests. Additionally, not all medical tests are ethically equivalent. Certain tests, such as pregnancy testing and HIV testing, may have complex social consequences and can lead to serious, avoidable harms.

Modern medicine is a science that incorporates theories that are expected to be consistent and generalizable. Although all data are deeply theory laden, the practice of evidence-based medicine (EBM) is founded on the concept that conscientious, judicious, and explicit use of the best available medical evidence should be integrated with clinical experience derived from systematic research in making decisions about the medical care of individual patients. In general, nonsystematic clinical experience, anecdote, and untested theory are not sufficient grounds for clinical decision making.

EBM and medical ethics share common principles and goals: both are aimed at maximizing benefits and minimizing risks, as well as at involving the patient in shared decision making. Using EBM to guide clinical testing and therapy is supported by analysis of traditional therapies that were never subjected to rigorous testing and that, on examination, were shown to be not only unhelpful to patients but possibly harmful. One Cochrane review, for example, found that administration of human albumin, a mainstay of therapy for treatment of shock, may be associated with increased mortality.<sup>34</sup> Another Cochrane review demonstrated that although mammography screening will prolong the life of 1 in 2000 women over a 10-year period, it will lead to the false diagnosis of cancer and the institution of cancer treatment in 10 women during that same period; these findings raise serious questions about the benefits and risks of routine mammography.<sup>35</sup> Using systematic evaluation of medical diagnostic testing to develop principles of preoperative testing not only serves the ethical principles of beneficence and nonmaleficence, but also permits us to provide patients with accurate and up-to-date information on the potential benefits of tests to aid their understanding and input in their medical care—thus honoring the principle of respect for the patient’s autonomy.

Conversely, EBM presents potentially significant ethical concerns. In relying on traditional medical experimentation, EBM may not sufficiently account for the role of social and cultural factors (e.g., poverty, ethnicity, spirituality, and gender) in health, and instead may rely too heavily on a narrowly drawn biomedical model of the patient’s experience of health and disease. In the words of Rogers, “those with the greatest burden of ill health are disenfranchised, as there is little research that is relevant to them, there is poor access to treatments, and attention is diverted from activities that might have a much greater impact on their health.”<sup>36</sup>

Despite its limitations, it nevertheless seems reasonable to believe that in trying to maximize beneficence and minimize nonmaleficence, EBM provides at least an improvement in the search for a rational, cost-effective approach to medical testing over simply adopting “traditional” therapies or protocols without evidence that they will contribute to accomplishing those goals. Applying medical tests inappropriately can cause very real harm to patients. Simply stated, if medical care is not valid, then it is not ethical.

Evidence that routine tests or traditional patterns of preoperative testing enhance perioperative outcomes is scant. Large population studies of many routine preoperative tests, such as coagulation screening,<sup>37</sup> chest radiography,<sup>38</sup> and electrocardiography,<sup>39</sup> have, on the contrary, found that these tests increase costs without necessarily positively affecting outcomes and can even lead to detrimental outcomes. The ASA Task Force for Preanesthesia Evaluation acknowledged that most routine testing is not necessary.<sup>40</sup> When evidence-based algorithms for preoperative testing are available and have been appropriately validated clinically, they should be used to guide clinical decision making.

## ROUTINE PREOPERATIVE PREGNANCY AND HUMAN IMMUNODEFICIENCY VIRUS TESTING

Social risks of preoperative testing may not be as obvious to the physician as medical risks, but they can be the source of significant harm. Examples of tests that can produce social harm and are of limited preoperative utility are HIV and pregnancy tests. Both tests have serious ethical consideration; have limited, if any, beneficial impact in the setting of surgery; may have serious social and economic consequences for the patient beyond the operating room; and require the patient's informed consent.

HIV tests are often ordered for the purpose of singling out patients for whom extra universal precautions could be taken to reduce transmission in the operating room. Most surgeons and anesthesiologists believe that compulsory HIV testing would reduce their risk of exposure, and many believe incorrectly that this testing is the physician's prerogative and can be done without the patient's consent.<sup>41</sup>

However, HIV testing does not necessarily yield safer anesthetic management and is more costly than diligent application of universal precautions.<sup>42</sup> In low-prevalence populations, testing is more likely to give false-negative results that wrongly reassure operating room workers that a patient is not infected. This may paradoxically increase the risk of HIV transmission if relaxation in vigilance is the result.

HIV tests can result in loss of employment, insurance coverage, or both. Seropositive women can experience marital breakup, abandonment, verbal abuse, and physical violence if their status is disclosed.<sup>43,44</sup> The threat of compulsory HIV testing almost certainly would prevent some patients from seeking needed surgical care.<sup>41</sup>

Routine preoperative pregnancy testing has ethical ramifications analogous to those of HIV testing. Despite pervasive beliefs to the contrary, studies do not conclusively demonstrate that anesthetic agents lead to early fetal loss, and no anesthetics have been clearly associated with teratogenic effects.<sup>44-47</sup> Studies have also shown that even adolescent girls generally accurately report the possibility of pregnancy when asked privately.<sup>48</sup> Legal ramifications of not routinely testing for pregnancy preoperatively have been virtually nonexistent, and fewer than one third of practices in the United States require such testing.<sup>49</sup> A positive pregnancy test may have extremely negative consequences if a vulnerable patient is in a social situation in which pregnancy is not accepted. Up to two-thirds of sexual assault victims are minors, and some are the result of child rape within the home. Abandonment, negative family interactions, and violence to the patient or

her fetus, or both, may all occur, as reactions to revelation of the pregnancy, attempts to hide a sexual domestic crime, or even in some cases as "honor killings."<sup>50</sup> Referral of pregnant adolescents to child protective services should be considered.<sup>49</sup> In many states, it is illegal to disclose or even insinuate a child's pregnancy status to her parents, regardless of her age. Therefore, the anesthesiologist who discovers an adolescent patient's pregnancy has few comfortable or legal options.

Many patients may choose not to undergo an elective surgical procedure if they know they are pregnant. However, *coercing* a female patient to have a test against her wishes and that she may find insulting explicitly violates the principle of the patient's autonomy. The physician's self-interest is not adequate justification for disregarding a patient's autonomy or violating a patient's privacy. The ASA Task Force on Preoperative Testing and the ASA Committee on Ethics jointly recommended that anesthesiologists offer the *choice* of preoperative pregnancy testing to any female patient who may desire it, explain the potential risks and benefits, and obtain informed consent or informed refusal for the test.<sup>40</sup>

## Ethics of Anesthesia Involving Pregnant Women

### MATERNAL-FETAL CONFLICTS

In general, the rights of pregnant women to refuse therapy, even if it will be detrimental to their fetuses, are protected under right-to-privacy provisions in the U.S. Constitution. Those rights are weighed against potential harms to the fetus in a decremental fashion as the fetus approaches and surpasses viable age. When the fetus is of nonviable age, the mother's rights prevail. Court decisions have consistently upheld the rights of pregnant women to have abortions, to not be subjected to drug testing, and to forgo transfusions early in pregnancy. Attempts to charge women with child abuse, child endangerment, drug trafficking, murder, and attempted murder for activities deemed dangerous to their fetuses have almost uniformly failed.<sup>51</sup> In general, women do not lose their rights to bodily integrity and informed consent when they become pregnant, and neither fetal "rights" nor state interests supersede a pregnant woman's right as medical decision maker.

The American Academy of Pediatrics Committee on Ethics outlined conditions that in their view are necessary to override a mother's refusal of care: (1) the fetus will suffer irrevocable harm without the treatment, (2) the treatment is *clearly indicated* and likely to be effective, and (3) the risk to the woman is low.<sup>52</sup> The American College of Obstetricians and Gynecologists condemned the use of coercion in pregnant women and advocated counseling the patient carefully about risks, as well as consultation with an ethics committee.<sup>53</sup>

### INFORMED CONSENT IN LABORING WOMEN

The validity of informed consent for epidural anesthesia in laboring women is a topic of concern to anesthesiologists, who periodically raise the question whether laboring women are able to consider and weigh the risks of labor

analgesia sufficiently while they are in pain. Although ideal conditions for informed consent are often lacking during labor, it is important to realize that the ideal is seldom achieved even in elective surgical patients; therefore, it is crucial to distinguish between conditions that are not *ideal* from conditions that are not *adequate*.

Despite concerns by anesthesiologists, most studies show that laboring women have the same capacity to give informed consent as the general surgical population,<sup>54,55</sup> are able to recall details of the consent process long after labor is finished, and indicate that labor did not alter their decision making.<sup>56</sup> Furthermore, studies show that the presence or absence of labor pain has minimal effect on a woman's ability to recall analgesia risks and other elements of the informed consent process later.<sup>55,57</sup> Some investigators argue that it is only after the patient enters active labor and she can assess for herself the severity of pain and consequences of proceeding without analgesia that she can be fully informed.<sup>54</sup>

An ethical conflict can arise in the case of so-called Ulysses directives in which, before labor, a woman executes an advance directive that refuses epidural analgesia and instructs doctors to ignore her pleas for epidural anesthesia at the time of labor should she change her mind. Although some experts suggest that ignoring the Ulysses directive disrespects a woman's long-term preferences, others argue that "information and valid experience are critical prerequisites for autonomous decision making" and that only the current wish (to receive an epidural) is ethically relevant.<sup>58</sup> Such cases appear to have no clear and unequivocal ethical ground on which to proceed, and circumstances must guide the physician. However, if an anesthesia practice decides to disregard Ulysses directives routinely, this should obviously be disclosed to patients in advance of labor whenever possible.

## The Uncooperative Patient—Coercion and Restraint

The use of physical restraint to control medical research subjects was first directly addressed in the Nuremberg Code following the Doctors' Trial in 1947 to 1949 and is a continuing subject of intense scrutiny.<sup>59</sup> For anesthesiologists, chemical restraints often replace physical ones, but the ethical issues are the same. Anesthesiologists are often asked by medical colleagues to chemically restrain uncooperative patients. Use of restraints is antithetical to promotion of autonomy, and anesthesiologists have both ethical and legal obligations to determine whether such extreme intervention is warranted. Coercing or using physical or chemical means to force a competent patient to undergo treatment that he or she is refusing is both unethical and illegal. Refusal of medical care and angry behavior are not proof of incompetence, intoxication, or inability to make medical decisions.<sup>60</sup>

When faced with the uncooperative adult patient, questions to ask include the following: (1) Is the patient clearly incompetent or merely angry and uncooperative? Does the patient show evidence of neurologic impairment, acute intoxication, or severe mental disability? (2) Is the patient in imminent danger? (3) Does the patient pose a direct

threat to staff or other patients? (4) Does a compelling need to treat life-threatening injuries exist? In the absence of any of the foregoing, the use of coercion or physical or chemical restraints is neither ethical nor legal. Physicians may be forced in some situations to act within a time frame that does not permit lengthy evaluation of a patient's competence or a protracted search for a surrogate decision maker. The standard applied in such cases would be to do what a "reasonable" person would wish. Coercion or restraint (or both) in such situations is not ideal, but it may be necessary and ethically permissible.

The uncooperative child presents special ethical concerns. When a patient who does not have the capacity to make healthcare decisions dissents from medical care, the anesthesiologist is ethically required to provide care that is most likely to benefit the patient and prevent harm while preserving the dignity and safety of the patient. Although violation of respect for autonomy is technically not possible in a patient who does not have autonomy, violations of principles of beneficence, nonmaleficence, and respect for dignity certainly are. Indiscriminate use of physical or chemical restraints is not without physical risk, and the fear and anger provoked by such tactics can lead to future aversion of medical care and mistrust of healthcare providers. The American Academy of Pediatrics Committee on Child Abuse and Neglect stated that restraint should not be used in pediatric care "unless it is necessary for proper diagnosis and treatment in a sick child, as in the case of a child with a high fever and potential ear infection, or in emergency situations."<sup>61</sup>

Behavioral control in the uncooperative child or incompetent adult should focus on alternatives to physical restraint, such as offering choices on how to go to sleep and use of fantasy or hypnotic suggestion. Despite many possible social, economic, and scheduling pressures to the contrary, delaying or rescheduling a surgical procedure in a hysterical patient is better than using coercion or force. Delaying elective surgery may reduce stress, allow adequate premedication, and promote safer induction conditions. If medical care is urgent, or if delay is unlikely to result in better conditions for the patient, then the anesthesiologist should proceed in a manner designed to preserve the patient's dignity and safety.

## Truth Telling—Disclosure of Errors and Apology

Nonmaleficence has been a foundational principle for the medical profession since the time of Hippocrates, and this principle draws no distinction between deliberate and unintended harms. Medical care is fraught with uncertainty, risk, and error. Harms resulting from unexpected complications, accidents, systems issues, and medical mistakes are to be avoided with equal diligence whenever possible.

Wu and colleagues defined a medical mistake as "a commission or omission with potentially negative consequences for the patient that would have been judged wrong by skilled and knowledgeable peers at the time it occurred, independent of whether there are any negative consequences."<sup>62</sup> Medical errors occur in 3% to 5% of all hospitalizations.<sup>63</sup> More than 40% appear to be preventable, and

more than 15% result in patients' deaths.<sup>64</sup> In 1999, the release of the Institute of Medicine's report *To Err Is Human* focused public and political attention on the terrible fallout of medical errors in the United States.<sup>65</sup>

Studies showed that 76% of physicians admitted to a serious medical error that they did not disclose to the patient,<sup>66</sup> and 22% of physicians indicated that they would not disclose an error that caused a patient's death.<sup>67</sup> Reasons cited for a physician's reluctance to disclose errors included personal shame, fear of loss of prestige in the physician's cohort, fear of direct reprisal, lack of experience in disclosing uncomfortable information, fear of causing further harm (emotional or psychological) to the patient and family, and fear of litigation. In many cases, legal advice to physicians has discouraged disclosure and apology in the erroneous belief that these tactics decrease medicolegal liability.

Obfuscating the root cause of a patient's complication when it is caused by a medical error is not difficult in the physician-patient relationship because the physician has unique expertise and is the recipient of unique trust. Furthermore, a minimum standard of disclosure simply does not exist. The Code of Ethics of the American Medical Association (AMA) states that patients have a right to be free of misconceptions about their medical condition and that physicians have ethical obligations to "inform the patient of all the facts necessary to ensure understanding of what has occurred."<sup>68</sup> However, the AMA Code of Ethics addresses only "harms" and not "errors," thus implying no duty to disclose medical errors that do not lead to harm. Although some experts state that physicians may have a lesser obligation to disclose harmless errors and/or "near misses," it is nevertheless arguable that they should consider doing so. The physician has little to lose, and such disclosures may enhance discussion of medical care with the patient and result in a strengthened doctor-patient relationship. Legally, some experts consider full disclosure of medical errors to be an extension of the legal principle underlying informed consent: "Clearly, if the patient is entitled to know the risks of a procedure and what could go wrong prior to giving their consent, it follows that they would be entitled to know if something has in fact gone wrong, regardless of whether it was unanticipated."<sup>69</sup>

Respect for patients' autonomy requires that we disclose mistakes that harm patients because in so doing we release patients from misconceptions about their medical past and enhance their ability to share decision making about their medical care. Disclosure prevents mistaken attribution by the patient of adverse consequences to noncontributory causes. Disclosure is usually necessary for informed consent for treatments to address complications of the error. Disclosure may enhance patients' trust in physicians. Moreover, disclosure may facilitate a patient's obtaining just and fair compensation for economic consequences of the injury, such as lost work and pay.

The concern that disclosure of errors to patients will increase litigation or decrease patients' trust, either in the doctor involved or in doctors in general, has not been borne out. Studies have suggested that full disclosure of a medical error reduces the likelihood that patients will change doctors, improves patients' satisfaction, increases trust in the physician, and leads to a more positive emotional response.<sup>70</sup> Studies also have demonstrated that patients

take legal action because they want more honesty from their physicians and assurances that the physician has learned from the mistake and that future patients therefore are less likely to suffer.<sup>71</sup>

An often-ignored aspect of medical errors is the effect that errors and disclosures have on physicians and other healthcare workers, who experience anxiety, fear, guilt, shame, self-doubt, anger, and disappointment. Damage to physicians, nurses, and others can be both long-lasting and severe, particularly following serious errors, manifesting as substance abuse and suicide. In a survey of anesthesiologists, 84% had been involved in at least one unanticipated death or serious injury, 88% stated they needed extended time to recover, with 19% stating they never fully recovered after the event. Twelve percent considered a career change. Even though 67% considered their ability to provide care was compromised in the first 4 hours following the event, only 7% were given time off. Five percent admitted to turning to drugs or alcohol as a coping mechanism.<sup>72</sup> Most anesthesiologists report inadequate support from colleagues or their institution in coping with such events.<sup>73</sup>

Physicians benefit from a sense of relief after disclosure and, at least in many cases, the forgiveness of the patient.<sup>74</sup> Disclosure helps physicians learn and improve their practice. Failures to report errors, learn from errors, and communicate errors and their potential solutions within a healthcare system are major causes of medical errors themselves. One could argue that a physician who does not disclose a preventable error, such that it is repeated, bears responsibility for harm not only to his or her own patient, but also to all future patients in whom the error could have been prevented had it been disclosed.

Disclosure can present some harm to the physician: disclosure is stressful, litigation may result, malpractice premiums may increase, and future employment may be adversely affected. However, in the doctor-patient relationship, ethical frameworks hold that benefits and harms to the patient should hold more weight than benefits and harms to the physician.

Do we have an ethical duty to disclose the errors of others? Legally, some North American courts have held that we do not,<sup>69</sup> and social norms about "tattling" on others are powerful deterrents to such disclosures. The reporting physician may hesitate because of a lack of definitive information, potential accusations of interfering in the doctor-patient relationship of another, worry that professional interactions such as patient referrals and performance evaluations may be affected, and fear of libel suits. When a physician observes a medical error committed by another physician, the options include nondisclosure, recommendations to the involved physician to disclose the error, disclosure of the error to a third party such as a risk-management group, or direct disclosure to the patient. Although no strict legal guidelines are in place, ethical principles favor actions that lead the patient to have a full understanding of what has occurred during his or her medical care.

Apology (as opposed to disclosure) remains a controversial aspect of communication following medical errors, largely because of fear that it could be used as an admission of negligence in subsequent litigation. Yet apology appears in many cases to decrease the risk of subsequent litigation, and lack of apology is a commonly cited reason among

malpractice plaintiffs for their legal action.<sup>75</sup> Spurred on by a desire to reduce litigation, many states have enacted “apology laws” that prohibit use of various types of apologies in court against physician defendants in malpractice cases. The impact of these laws and the impact of apologies on the incidence and outcomes of malpractice litigation remains unclear, although significant numbers of patients who have sued physicians indicate that an apology would have prevented them from doing so.

## ADVANCE DIRECTIVES AND SURROGATE DECISION MAKERS

Critical decisions regarding medical care often arise when patients are too ill to formulate or express decisions regarding medical interventions. *Advance directives* were developed after several legal decisions affirmed that patients can refuse even lifesaving medical care and that clear and convincing evidence of the patient’s wishes is needed to allow surrogate decision makers to request withdrawal of life-sustaining therapies.<sup>76</sup> An advance directive is a document executed by the patient before incapacity to provide the patient’s physicians with guidance when the patient cannot communicate for himself or herself. Such directives include the following: living wills, which detail the therapies a patient would accept or refuse in the case of terminal incapacity; DNAR orders; and any other preferences regarding medical care decisions.

A surrogate decision maker is someone whom the patient has appointed to make healthcare decisions for him or her (a durable power of attorney [durable POA]) or an individual with other legally recognized authority by virtue of his or her relationship with the patient.

A durable POA for healthcare decisions may be given by the patient to a specific person he or she designates to make healthcare decisions for them if they become incapacitated. The authority vested in a POA supersedes most other decision makers, including family members, except a court-appointed guardian.

When the patient has not designated a durable POA, doctors rely on family members to make decisions for the patient. Many states have a legally defined hierarchy of decision makers. Commonly, the surrogate hierarchy is the spouse or legally recognized domestic partner, followed by the children, if all are in agreement, then parents, if both are in agreement, and then siblings, if all are in agreement. The anesthesiologist should familiarize himself or herself with the specific laws of the state in which they practice.

Surrogate decision makers are explicitly trusted to act in “substituted judgment” to provide what the patient would have wanted and theoretically are not asked merely for their own preferences. However, surrogate decision makers at best only approximate the patient’s decisions because their interpretation is subject to their own biases, values, and psychological agendas. Incompetent patients can be emotionally and financially burdensome, and decision makers may have conflicts of interest that distort their beliefs and testimony about what the patient would have wanted.

Studies demonstrate that patients and their proxies only infrequently discuss issues and values involving life-sustaining technologies. Discrepancies between patients and proxies are often significant in the assessment of

patients’ emotional health and satisfaction. Neither physicians nor proxies can always accurately predict the patient’s preferences for life-sustaining therapies.<sup>77,78</sup> Nevertheless, with all the imperfections, proxy decision making may be the only option if a patient has not left specific directives.

## Medical Decisions That May Require a Court Order

Some medical treatments have intense cultural connotations, may involve limitation on private freedoms such as reproduction, or may have historically been subject to abuse. Decisions regarding these interventions *cannot* be made by a surrogate decision maker (even if one is available) and require a court review. Examples of such treatments in many states include sterilization and electroshock therapy.

The anesthesiologist should review the patient’s record before taking the patient to the operating room and ascertain (1) whether the patient has advance directives, (2) who the patient’s surrogate decision makers are, (3) whether the procedure is legally allowed with consent from a surrogate decision maker, and (4) in special cases, whether an appropriate court order has been obtained.

## Do-Not-Attempt-Resuscitation Orders in the Operating Room

Up to 60% of anesthesiologists wrongfully believe that DNAR orders are automatically suspended during anesthesia and surgery. The ASA,<sup>25</sup> the American College of Surgeons,<sup>79</sup> the Association of Operating Room Nurses,<sup>80</sup> and The Joint Commission<sup>81</sup> all published practice guidelines requiring reconsideration, not abandonment, of the DNAR orders in the perioperative period.

The causes and outcomes expected with a cardiac arrest in the operating room are different from what may happen outside the operating room, although they are still poor, with a “viable” survival of only about 25%.<sup>82</sup> It is important, therefore, that patients be informed of the risks and benefits of cardiac resuscitation so that they can best determine whether to ask for their DNAR order to be suspended during the perioperative period.

Although the patient’s primary care physician may have introduced the idea of DNAR orders to the patient or the surrogate decision maker, it is the anesthesiologist’s duty to discuss the risks and benefits of resuscitation in the setting of anesthesia and surgery before undertaking the patient’s care. The anesthesiologist should include in this discussion the following steps: (1) determine the patient’s goals regarding surgery and resuscitation; (2) establish exactly what is meant by “resuscitation,” in contrast to routine anesthetic care; (3) educate the patient about the risks and benefits of resuscitation in the operating room setting; and (4) document the agreements reached with the patient about which interventions commonly associated with resuscitation are acceptable to him or her. Such interventions could include, but are not limited to, intubation, administration of vasoactive drugs, administration of direct current countershock, and institution of chest compressions. Many patients who express reluctance about resuscitation during surgery actually most fear burdensome collateral outcomes, such as permanent neurologic impairment, rather than the process of resuscitation itself. Education and discussion may reassure these patients about the potential outcomes of resuscitation

in the operating room and can establish ground rules for discontinuing interventions postoperatively if they do not lead to a chance of meaningful recovery.

Surgery depends on the cooperation of many caregivers with differing expertise, each with independent ethical obligations to the patient. Resuscitation agreements must be discussed with other members of the operating room team. This communication prevents crucial disagreements from occurring during a critical event when treatment decisions must be made quickly. It also allows “conscientious objectors” to withdraw from the healthcare team.

Advance directives are legally and ethically binding. Despite clear, consistent, and forceful legal decisions, physicians have ignored DNAR directives under the false assumption that the legal authority of advance directives and living wills is not binding in the operating room or that the physician has discretion in deciding when to follow or ignore such directives—and families have sued for significant monetary damages for the costs of continued health care and punitive damages for the pain, suffering, and mental anguish of the patients’ survivors when DNAR instructions are ignored.<sup>83,84</sup>

In 1990, the U.S. Congress passed the Patient Self-Determination Act that recognizes a competent patient’s right to refuse any medical therapy, including life-sustaining therapy, and requires medical institutions and providers to advise patients of these rights and ask about their preferences.<sup>76</sup> Compliance with the act is required in order to participate in Medicare and Medicaid reimbursements. Furthermore, in 2006, the American Civil Liberties Union filed suit against a group of New Mexico orthopedic surgeons who were requiring patients to sign away their rights to DNAR as a requirement of surgery, arguing that this not only violated the 1990 Patient Self-Determination Act, but denied patients their constitutional rights. The surgeons were required to desist in that practice, publicize the change in policy (to respect DNAR), and pay attorneys’ fees and various other fines.<sup>85</sup>

Finally, DNAR orders must never be construed as an excuse to not “care” for the patient. A patient’s decision to forgo resuscitation does not imply a wish to avoid other beneficial interventions. Placement of a pulmonary artery catheter, for example, may help ensure optimal management of a frail patient who has a DNAR order and enable the anesthesiologist to avoid situations in which the patient’s DNAR status becomes pivotal.

## END-OF-LIFE DECISION MAKING

A 1996 review by the AMA showed that the following end-of-life issues were of foremost importance to patients: control over the timing and location of death; management of symptoms such as pain, dyspnea, anxiety, and depression; financial management of medical care; and maintenance of therapeutic options, including physician-assisted suicide (PAS).<sup>86</sup>

### Withdrawal or Withholding of Medical Therapies

Between 2000 and 2010, about one-third of deaths in the United States occurred in short-stay general hospitals.<sup>87</sup> Patients and doctors alike recognize that aggressive medical therapy may not be desired or even appropriate in the

presence of advancing disease, and over time the use of hospice and palliative care facilities has increased.<sup>88</sup> Most deaths in ICUs occur after an explicit decision to withdraw or withhold treatments.<sup>89</sup>

Before the mid-20th century, the concept of beneficence in the eyes of physicians was strongly tied to preventing death. Ethical distinctions between acts of omission (“letting die”) and acts of commission (“killing”) were and remain confusing at best. Worse, physicians faced threats of criminal punishment if a patient’s death resulted from withdrawal of medical treatments.<sup>90</sup> In 1976, the case of Karen Ann Quinlan established that patients have a right to forgo invasive treatments, even if lifesaving, and that surrogate decision makers could ask for withdrawal of lifesaving therapies if the surrogates could show that the patient would not have wanted them.<sup>91</sup> The right to forgo lifesaving treatments was later extended in the cases of Claire Convoy and Nancy Cruzan to include *any* treatment if the patient refused it or if clear and convincing evidence indicated that the patient would have refused therapy if he or she could speak for himself or herself.<sup>76</sup> These decisions were revisited and reconfirmed in the tragic case of Theresa Schiavo in 2005.<sup>92</sup>

Arguments that withdrawing or withholding life-sustaining therapy does not violate rules against killing patients are based on ethical differences between killing and letting die, and between acts of commission (e.g., lethal injection) and acts of omission (e.g., withdrawal or withholding of ventilator therapy).<sup>93</sup> Because such distinctions are confusing to both physicians and patients, a *principle of proportionality* is often applied when withholding or withdrawing treatments.<sup>94</sup> In this principle, treatment is indicated to the extent that it is likely to present more benefits than burdens to the patient based on the patient’s perception of such medical, social, and psychological benefits and burdens. Of course, competent patients still always have the right to refuse therapy, even if lifesaving and otherwise indicated.

Two common settings in which anesthesiologists may be involved in withdrawing or withholding life-sustaining interventions are the ICU and the operating room before organ donation after cardiac death (DCD). In both cases, the issues and principles of withdrawing or withholding treatments are the same.

Withdrawal of life-sustaining interventions heralds the final phase of end-of-life care, and it is a socially critical phase in the life of the patient and family. Terminal care requires special knowledge and experience on the part of the physician. It requires expertise in medically supportive therapy, management of problematic symptoms, knowledge about physiologic changes in the dying patient, support and counseling of patients and families, understanding and respect for the patient’s autonomy and religious and cultural practices and beliefs, the ability to work within complex healthcare teams, the ability to communicate well, and empathy. Anyone intimately involved in care of the dying patient should also be intimately familiar with ethical and legal standards.

Withdrawal of life-sustaining treatment begins with an assessment of the individual patient’s physiology, level of dependence on therapy, degree of consciousness, preferences regarding sedation and analgesia, and preferences

regarding privacy and level of involvement of family and other loved ones. All the patient's treatment orders should be reviewed to meet the new treatment goals. Treatments promoting the patient's comfort should generally be continued, whereas those directed only at physiologic maintenance may all be withdrawn. Family members and others attending the patient at the end of life should be educated about physical and mental changes they can expect to see as treatments are scaled back, including the possibility that death will not occur imminently once support is withdrawn.<sup>95</sup>

Several interventions have ethical implications and deserve special consideration—fluid and nutritional management; the administration of sedatives and narcotics that have the potential to hasten death; the administration of neuromuscular blocking drugs; and deactivation of pacemakers, ventricular assist devices, and implantable cardioverter-defibrillators (ICDs).

The issue of fluid and nutritional support is controversial. Burdens associated with continuation of fluid and nutritional support include prolongation of the dying process, and complications and suffering from placement and maintenance of intravenous or enteral access (or both). However, feeding and hydration may have important connotations for family members and members of the health-care team by allowing a sense of nurturing and mitigating feelings that they are "abandoning" the patient.<sup>95</sup>

Pain, dyspnea, and depression are all common symptoms that cause suffering in the dying patient. Alleviating pain and dyspnea carry the risk of hastening death. Medical, legal, and religious authorities have all clearly accepted the principle of "double effect," in which an action intended to produce a benefit for the patient produces not only the expected benefit but also the potential for significant harm. It is entirely ethical and legal to administer high doses of pain medication and sedatives for the intended effect of relieving suffering, even if the treatment has the side effect of hastening death. However, to administer any medication with the explicit intention of hastening death is euthanasia, and not medical therapy.<sup>95</sup>

## TERMINAL SEDATION

"Terminal Sedation," also known as "deep continuous sedation" (DCS), is an ethically controversial end-of-life strategy for patients who are suffering intolerable symptoms in the last stages of dying, and who do not respond well or completely to sedatives or pain medications that are being administered "as needed" in response to symptoms. In DCS, a decision is made with the patient or their appropriate surrogates to forgo reactive treatment of symptoms and to employ intravenous sedative/analgesic infusions with the intention of rendering the patient permanently unconscious until death occurs, but without the intention of causing death. While the goal of DCS—relief of suffering—is a laudable one, ethical questions nevertheless persist: the practice is plagued by vague and nonstandardized terminology and practice, a lack of outcomes research, an uncomfortable confusion with PAS and euthanasia, misunderstanding of the principle of double effect, and culturally diverse philosophies about the role of suffering and transcendence in the meaning of human life.<sup>96</sup> Opponents

suggest that DCS is merely euthanasia in disguise, invented to circumvent legal sanctions and moral objections. Some ethicists have argued that DCS permanently deprives the patient of morally relevant aspects of "personhood" and therefore represents a form of killing. Disturbing studies show that many physicians employing DCS actually *do* intend to hasten death.<sup>97,98</sup>

A particularly controversial aspect of DCS is whether it can and should be allowed when the patient is suffering from severe and intractable *existential* suffering: fear, loneliness, anxiety, spiritual crises, and so forth. Professional guidelines regarding DCS and existential suffering at end of life differ greatly in their recommendations: the American Academy of Hospice and Palliative Medicine<sup>99</sup> and the American College of Physicians<sup>100</sup> do not make specific statements about DCS in existential suffering; the AMA Council on Ethical and Judicial Affairs opposes DCS for existential suffering;<sup>101</sup> the Royal Dutch Medical Association<sup>102</sup> and the Harvard University Community Ethics Committee<sup>103</sup> support the use of DCS in cases of existential suffering; and the Veterans Health Administration does not exclude it, but weighed against use of DCS for existential symptoms in their discussions.<sup>104</sup> Even more questions arise when DCS is instituted in pediatric patients.<sup>96</sup>

## NEUROMUSCULAR BLOCKING DRUGS

Neuromuscular blocking drugs have no anesthetic, analgesic, or sedative properties. Such drugs should not be initiated if withdrawal of ventilatory support is anticipated. Paralyzing the patient to comfort *the family* so that they see no disturbing movements or respirations as the patient dies is not justifiable. Even worse, it can mask symptoms and signs of distress and can thus prevent relief of suffering during the dying process.<sup>95</sup> When withdrawal of ventilator support is anticipated in a patient already receiving such drugs, they should be withheld in all but extraordinary cases.<sup>105,106</sup>

## IMPLANTABLE CARDIAC DEVICES

When a patient who has a cardiac device requests withdrawal of life-sustaining interventions, questions can arise about whether it is ethical to deactivate or even explant such devices at the patient's request. In the case of ICDs, the question might well be whether it is ethical to *continue* such therapy in a patient who has opted for palliative care. Recent studies provide concerning information: in the MADIT II trial, only 15% of patients who died had their ICD deactivated, after receiving "many" shocks at the last days of their lives.<sup>107</sup> A post-mortem device interrogation study indicates that 31% of patients received shocks in the last 24 hours of life.<sup>108</sup> It is likely that patients receiving shocks in the final hours of their lives may be unable to communicate that they are suffering this painful experience and ask to have it stopped. In another study, only 27% of patients had discussed deactivation of the ICD at end-of-life,<sup>109</sup> raising concerns that failure to deactivate the device was due largely to failure of physician-to-patient communication that this was possible and should be considered. In some cases, physicians may lack the expertise or equipment to promptly deactivate such devices when inappropriate shocks are being delivered.<sup>110</sup>

Some experts have said that that these devices must be treated differently from other medical interventions because by virtue of implantation they have become a “biofixture,” or literally a part of the patients themselves.<sup>111</sup> Such arguments are difficult to sustain when we consider that many people undergo implantation of medical devices and subsequent explantation of them when the devices are no longer working or do not serve the patient’s purpose. Common examples include artificial joints, intraocular lenses, medication delivery devices, and orthopedic hardware. Furthermore, these devices are never uniquely a part of the patient in the same sense as DNA or their native organs. In fact, the ethical distinction between disabling a pacemaker in a pacer-dependent patient and turning off a ventilator for a ventilator-dependent patient is minimal if the request comes from a competent patient or the surrogate decision maker. Both actions involve discontinuance of artificial therapies that the patient no longer desires, and both may be followed by rapid death.

Consensus statements and guidelines by the Resuscitation Council of the UK, British Cardiovascular Society, and National Council for Palliative Care,<sup>112</sup> the European Heart Rhythm Association, and Heart Rhythm Society,<sup>113</sup> and the Canadian Cardiovascular Society<sup>114</sup> all recommend discussion with the patient of deactivation of implantable cardiac devices in end-of-life care.

The presence of a do-not-resuscitate order should not be taken as an automatic request by the patient to discontinue implantable device therapy. As with other end-of-life therapies, discontinuance of such devices should include due consideration of whether the decision is made by a competent patient and with full informed consent. Management of discontinuance of device therapy should always include planning for treatment of distressing symptoms and administration of appropriate comfort measures.

## PHYSICIAN-ASSISTED SUICIDE AND EUTHANASIA

PAS is defined as the provision of medication or prescriptions by a physician to a patient at their specific request for the explicit purpose of ending their life. PAS requires a patient who is both competent and capable of communicating the request, as well as capable of self-administration. Euthanasia is defined as the administration of medication by someone other than the patient for the express purpose of causing death in the belief that this would be best for the patient, but not necessarily at the specific request of the patient. Both practices differ ethically from withdrawing or withholding life-supporting medical treatments. In withdrawal or withholding of life-supporting treatment, the primary intention is to discontinue treatments that are causing suffering with an understanding that death may or probably will result. In PAS and euthanasia, the primary intention is to cause death, which secondarily ends suffering.

Currently, euthanasia is legal only in the Netherlands, Belgium, and Luxembourg. Some confusion exists about the status of euthanasia in Colombia, which has been labeled as allowing “euthanasia,” but appears in fact to have legalized PAS, reflecting a common misconception in the press about differences between the two practices.<sup>115</sup> In the United States, euthanasia remains illegal regardless

of circumstance, but PAS is legal as of 2018 in the states of Oregon, Washington, Montana, Vermont, Colorado, California, and the District of Columbia. It narrowly missed ratification in New Mexico after being passed by both state houses in 2017, and it passed the Hawaii State House of Representatives in March of 2018. It is also under consideration in other states. Thirty-seven states have specific laws that make PAS illegal, and four states have no specific laws regarding PAS.<sup>116</sup> Internationally, PAS is legal only in the Netherlands, Belgium, Luxembourg, Germany, and Switzerland.<sup>117</sup>

Supporters of PAS argue that the right to privacy and respect for autonomy support a patient’s right to determine the time, location, and circumstance of his or her own death. Patients consistently rate loss of autonomy and control, inability to pursue previously valued activities, and loss of dignity as the major concerns at the end of life. Adequate control of pain, anxiety, dyspnea, and other symptoms at the end of life remain a challenge to the medical profession, thereby fueling the desire for a means to end life when suffering cannot be controlled. Opponents argue that PAS “medicalizes” death, overly idealizes the physician-patient relationship, ignores possible personal and professional conflicts of interest, and leads to erosion of trust between dying patients and their doctors. Although many ethicists acknowledge that individual circumstances may make assisted suicide an ethically permissible action, most express concerns about potential abuse. Vulnerable members of society, such as the poor, old, and handicapped, could be pressed by financial and social factors into a suicide option in preference to palliative care. An additional argument against PAS or legalized euthanasia is that these approaches could provide solutions to the medical, social, and economic problems common to older and poor patients that are simpler and less expensive than seeking and requiring more difficult but definitive remedies.

Twenty years have passed since Oregon legalized and enacted PAS in 1997 and the Netherlands legalized both PAS and euthanasia, and significant data now provide some insights into whether these concerns about PAS and euthanasia are materializing. In recent polls, more than two thirds of the U.S. population polled favored legalizing PAS, and approximately 70% favored legalization of euthanasia.<sup>118</sup> The percentage of U.S. oncology patients favoring a PAS or euthanasia option in end-of-life care is approximately 65%,<sup>119</sup> whereas physicians frequently involved in end-of-life care, such as intensive care specialists, oncologists, and palliative care specialists, are the most uniformly opposed specialists.<sup>120</sup> This finding represents a significant discordance between physicians and their patients.

In Oregon, where PAS has been legalized for the longest period in the United States, data from 2015 (the most recent year available) remain consistent and show that patients who requested PAS were more likely to be white and had generally higher economic status and education. More than 99.2% were insured, and 92.2% were enrolled in hospice care. Most were more than 65 years old (78%), and 72% were suffering from cancer. As of 2015, 36% of patients receiving prescriptions for PAS (a total of 1545 patients over 20 years) never used them and ultimately died of their underlying disease—with many surviving significantly longer than predicted. More than 92% of patients

enrolled in the Oregon program cited loss of autonomy as a primary reason for pursuing the option.<sup>121</sup> Some authors have suggested that the possession of a means to end their lives legally and humanely prevented “preemptive” suicides that could have occurred earlier and thus may have prolonged lives.<sup>122</sup>

Concerns regarding abuses of PAS and euthanasia will undoubtedly continue, but thus far, evidence of systematic abuse is lacking in places where PAS is legalized and regulated. As the population ages and patients desire greater control over end-of-life care and circumstances, debate over PAS and euthanasia in the United States can be expected to continue to grow.

## ETHICAL ISSUES IN ORGAN TRANSPLANTATION

Two issues critical to vital organ transplantation that confront anesthesiologists are the concept of brain death and the linkage of withdrawal of life-sustaining therapies with organ retrieval and transplantation after cardiac death (DCD).

### Brain Death

Before the 1960s, death was defined as the moment when the heartbeat stopped and respirations ceased. Advances in cardiopulmonary resuscitation and mechanical ventilation then made it possible to postpone death, seemingly indefinitely. In 1968, the Ad Hoc Committee of the Harvard Medical School proposed redefining death as the point at which all cardiorespiratory function had irreversibly ceased, or all function of the whole brain had irreversibly stopped (brain death).<sup>123,124</sup> The committee gave two explicit reasons for redefining death. The first was to allow patients to be declared dead and not maintained on machines—thus limiting expense; reallocating medical resources to other, salvageable patients; and allowing the social rituals surrounding death to occur. The second was to allow the donation of vital organs before circulation stopped.

Declaration of death further carries nonmedical consequences, such as the process of mourning, initiation of any criminal prosecutions, inheritance, taxation, and burial concerns. It was thus considered important that determinations of death follow consistent rules across state boundaries, and the National Conference on Uniform State Laws issued the Uniform Definition of Death Act in 1980, which was adopted by the states.<sup>124</sup>

The public has been slow to accept brain death, in part because it requires complete trust in physicians and ignores indicators of death that the public already understands. To nonphysicians, brain-dead donors are superficially indistinguishable in many ways from living persons, and nonphysicians must therefore rely completely on the physician for both accurate and honest information of a loved one’s death. Recent court cases challenging declaration of death in patients who clearly did meet standard brain death criteria, such as that of Aden Hailu in Nevada, illustrate continued public uncertainty.<sup>124</sup>

Medical standards in diagnosing brain death are relatively straightforward, although variations in the definition of death itself persist throughout the United States.<sup>124</sup> In the United States, medical standards require demonstration that, in the absence of drugs, paralytic agents,

hypothermia, and other reversible conditions that mimic loss of brain function, no cortical or brainstem function is present. The diagnosis is usually made either clinically, by demonstrating that cortical activity and brainstem reflexes are absent, or by radiographic studies demonstrating the complete absence of cerebral blood flow.

Although brain death is a *social* and not a *biologic* definition of death, medical, ethical, theological, and legal experts generally agree that brain death adequately defines a condition in which a person with ethical and legal rights and moral standing ceases to exist and should no longer be treated as though alive. Expensive medical interventions can be discontinued without legal ramifications, and vital organs can be donated for transplantation if the patient or the surrogate decision maker agrees.

Before assuming care of a brain-dead organ donor, the anesthesiologist is obligated to review the chart for documentation of the declaration of brain death and the criteria on which it was based. If any questions exist about the diagnosis, organ donation should be postponed until the anesthesiologist is satisfied that these concerns are addressed.

### Donation after Cardiac Death

DCD occurs when a patient wishes to have life-sustaining medical therapies withdrawn and also wishes to proceed with vital organ donation after death. Controlling the time and place of death so that timing of organ donation can be optimized has obvious medical and ethical advantages. The decision to donate organs is made before death, thereby allowing time for discussion and informed consent. Organ ischemia time can be minimized. The dual decision to withdraw life-sustaining interventions and donate vital organs after death can create ethical conflicts, however. When a dying patient becomes an imminent organ donor, the risk is that the patient’s interests will be minimized or ignored in favor of the organ recipient.

The National Academy of Medicine reviewed DCD in 1997<sup>125</sup> and 2000<sup>126</sup> and found serious ethical questions, such as determining how quickly after asystole organ donation can begin and whether medications can ethically be administered to the donor before death that are solely for the purpose of organ preservation.

Ethical, theological, and legal principles prohibit us from killing one person to benefit another, but the point at which actual death has occurred in DCD donors is unclear. Although expedient donation is the very purpose of DCD, doctors must never sacrifice any living patient in the process or even take significant risks of doing so; the mistrust this would engender among the public could place the entire concept of DCD at risk by reducing potential donors and ultimately harming future potential organ recipients.<sup>127</sup> Loss of consciousness occurs quickly after asystole, but brain function can continue for some time, and irreversible brain injury may not occur for many minutes. Yet some protocols call for organ retrieval to begin only 2 minutes after circulation has stopped, and in at least one institution, organ harvest is allowed to begin within seconds of cardiac arrest.<sup>128</sup> Scientific and philosophic uncertainty exists about when death is complete—this could even lead to accusations that physicians deliberately kill patients to obtain organs for transplantation. Mistakes have occurred in some cases of brain-dead organ donors for which clear

clinical criteria exist; DCD organ donation is potentially even more prone to error because no such clinical guidelines are universally accepted.<sup>129</sup>

Donation of vital organs after brain death and DCD are both ethical and legal, but the interests of the dying patient must be absolutely protected until after death has occurred. Anesthesiologists can play a vital role in the organ donation process by helping hospitals develop reasonable and ethical policies for the management of brain-dead donors and DCD donors. Every anesthesiologist should be thoroughly familiar with brain death criteria and should review the process of brain death determination before accepting care of a brain-dead donor. It is inappropriate for anesthesiologists to be involved in organ DCD unless they have expertise in the relevant ethical, legal, and medical issues and are experienced in end-of-life care.

## Research Ethics

### HUMAN SUBJECT RESEARCH

The premise that the physician always puts the best interests of the patient first can be jeopardized when research objectives enter the doctor-patient relationship. Human subjects are asked to put aside their own interests to benefit some future, hypothetic group of patients. In extreme cases, the patient becomes a research “object” who will not benefit personally from the experiment at all. Two examples include experiments in healthy subjects and phase I cancer trials in terminally ill patients in which the goal is to determine the toxicity of treatment—not remission, palliation, or cure.

Human subject research must balance many conflicting interests, such as the needs and rights of the research subject, the hypothetic interests of future patients, and the physician’s financial, professional, and personal goals. Academic or corporate advancement, personal prestige, and financial incentives may be disincentives to researchers who diligently protect patients’ interests or who remain objective in designing protocols and analyzing and reporting their findings. Thus, human subject research is more closely regulated, supervised, and controlled than any other medical endeavor.

Regulation of research began after World War II, with the Nuremberg Code and the Helsinki Declaration outlining the ethical obligations of physicians engaged in human research. The United States was slow to awaken to the parallels between the concentration camp experiments and the sometimes gruesome treatment to which they subjected their own subjects in similar trials.<sup>130</sup> In the years that followed the Doctors’ Trial at Nuremberg, Fox<sup>131</sup> and Beecher<sup>132</sup> found that researchers were aware of the standards set at Nuremberg but regularly did not comply with them. In 1974, the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, out of which the modern institutional review board was born.

The ethical conduct of human subject research follows three principles: (1) respect for autonomy and the obligation to protect subjects with limited autonomy; (2) beneficence, with obligations to minimize risks, maximize benefits, and

ensure that the research design is scientifically sound; and (3) justice, the obligation to treat each person with regard to what is morally right and to ensure fair distribution of benefits and burdens.

In addition to the comprehensive presentation to research subjects of the risks and benefits of procedures or medications to which they will be subjected, disclosure must include the possibility of commercialization of the results, financial interests of the researchers, and any other actual or perceived conflicts of interest on the part of researchers and their institutions and sponsors. Subjects must be free to refuse or end participation at any time without penalty. *Situational coercion*, in which subjects feel that they are not truly free to refuse, should be avoided or mitigated. Examples of situational coercion include prisoners whose terms and experiences of incarceration may be affected by their decision to participate or refuse, and hospitalized patients who may believe that their care could be compromised if they do not cooperate with researchers.<sup>130</sup>

Monetary or other inducements to participate in research are probably permissible if they do not undermine the freedom of the subject to refuse under reasonable circumstances. Significant monetary awards may have adverse effects on the autonomy of subjects and may negatively affect the scientific quality of the research. If remuneration is high, for example, subjects could conceal factors that would otherwise disqualify them from participating, thus compromising the research results and exposing themselves to greater risks.

Researchers are obligated to maximize benefits and minimize potential harms, including physical, psychological, social, legal, and financial harms. The research must address a question of significant value to justify the level of risk and must follow the approved protocol. Findings must be promptly and accurately reported. The research must be terminated immediately if it is suspected to be harmful to the participants.

Anesthesiology research often involves the treatment or prevention of unpleasant symptoms, such as pain and nausea. When effective treatments are well established, such studies should be restricted to comparison of treatments with known efficacy, not placebo-controlled trials, and “escape” analgesics or antiemetics must be provided on the patient’s request.

No population group should be unfairly subjected to research without having equal access to its benefits. Finally, the interests of the individual must always prevail over the interests of society.

### Children as Research Subjects

Children are particularly vulnerable as research subjects because they may lack the ability to make mature decisions, are subject to the authority of others, may defer to their parents and others in ways that mask underlying dissent, and may have conditions requiring immediate decisions not consistent with informed consent.<sup>133</sup> Children’s rights are frequently undervalued, whereas parental authority may be overvalued. Studies show that even children with decision-making capacity are often excluded from the consent process by both parents and physicians.<sup>134</sup>

If a minor child is “able” to assent, then assent must usually be obtained in addition to the consent of any legal

surrogate decision makers. In the United States, federal law requires assent of any minor age 7 years and older to participate in medical research. Particularly for research in which no substantive individual benefit is expected, many ethicists believe that a child's dissent *must always be honored*.<sup>134,135</sup>

## ETHICS OF ANIMAL RESEARCH

The animal rights movement in the United States has gained significant momentum since the 1980s, following in the wake of the U.S. civil rights movement and paralleling increasing awareness and concerns about the human impact on the environment and other animal species. In 1959, William Russell and Rex Burch published their sentinel book regarding the ethics of animal research, *The Principles of Humane Experimental Technique*, introducing the concept that humane treatment of animals was not merely an ethical imperative, but absolutely necessary to high-quality research.<sup>136</sup> Federal legislation protecting animal welfare began with the Laboratory Animal Welfare Act of 1966. In 1985, the Health Extension Act and amendments to the Animal Welfare Act required the establishment of Institutional Animal Care and Use Committees, which oversee conditions of laboratory animals; review and approve animal research protocols; educate and train investigators in ethical issues and aspects of animal handling such as anesthesia, analgesia, and euthanasia; and act as community liaisons.

Some researchers deny that animal experimentation could be subject to any moral reservations and assert that medical advances have been and continue to be completely dependent on continued animal research. Many animal welfare activists insist on the moral equivalence of animal experimentation to that of human experimentation and accuse researchers of being blind to or, even worse, actually unmoved by the suffering of animal subjects. The simplicity of these polarized views does not do justice to the complexity of the issues.

Advances in the understanding of animal cognition led most biologists to believe that many, if not all, animals are capable of feeling pleasure, pain, anticipation, and fear, and thus experience both enjoyment and suffering. Many bioethicists state that the higher animals therefore have adequate awareness to possess moral standing, although how much moral standing is intensely debated.<sup>137,138</sup> Allowing animal suffering as a result of pain, fear, sickness, or poor standards of care is a moral harm that must be avoided, mitigated, and weighed heavily against the benefits it produces. Ethicists maintain that cruelty to animals is immoral and that animals should be protected from it, not merely because they have moral standing, but because he who is cruel to animals is more likely to be cruel to humans.<sup>139</sup>

Researchers have obligations to provide clean and humane conditions and appropriate veterinary care for animal subjects. Researchers should mind the "Three Rs"—replacement, reduction, and refinement—that is, use animal subjects only when necessary, minimize any suffering incurred in the study, and seek nonanimate replacements for animal subjects.<sup>99</sup> Mediocre or repetitive research using animal subjects should not be allowed. It is the responsibility of the medical and scientific community to continue aggressively to seek and promote alternatives to the use of animal subjects.<sup>139</sup>

## PHYSICIAN PARTICIPATION IN EXECUTIONS

U.S. professional organizations for physicians have consistently stated that physicians' participation in executions is unethical, yet many physicians admit that they would agree to be involved. The role of physicians in euthanasia and executions is of particular concern to anesthesiologists, who have been identified as ideal candidates for duties that involve killing because of their particular professional skills. Arguments in favor of physicians' involvement in executions usually cite the principle of beneficence in allowing a humane death.

Historically, however, beneficence arguments have led to "slippery slope" justifications for physicians to be involved in the killing of persons who have never faced an accuser or had a fair hearing—such killings have included persons with physical or mental handicaps and other "social flaws" for the "benefit" of the individual and of society as a whole. Once physicians accept a beneficence argument for participating in executions, it is difficult ethically to draw the line at participating in other state-sponsored activities, such as torture, coercion, and "medical incarceration," because these activities are also usually defended as being beneficial to society.<sup>140</sup>

When physicians agree to participate in an execution, they act as agents of the state while appearing to act on behalf of the "patient." This situation can lead to eventual erosion of public trust and respect. It also at times undoubtedly leads to physicians' participation in the killing of innocent persons.<sup>141</sup>

To avoid intolerable self-condemnation, virtually all executioners undergo "moral disengagement" in which they dehumanize the convicts and devalue their lives, thereby deflecting moral responsibility for the execution away from themselves by blaming juries, judges, governors, and "the law" rather than accept the responsibility they share in ending the prisoner's life.<sup>142</sup> It is difficult to reconcile the medical profession's overt ethical imperatives of valuing human life, respecting individuals, and accepting personal moral responsibility with participation in a process that requires a rejection of these very values.

In 1980, the AMA issued an opinion that physicians' involvement in capital punishment is unethical and defined "participation" broadly as including not only actions that themselves would lead to the death of the condemned but also any activity that assisted, supervised, or contributed to another's being able to do so.<sup>143</sup> However, no direct sanctions of any participating physician were addressed. In 2010, the American Board of Anesthesiology became the first organization of physicians not only to condemn participation in capital punishment as unethical but also to state that physicians who were certified by their board and who participated in lethal injection would be subject to disciplinary action that could include revocation of their diplomate status.<sup>144</sup>

## MORAL INTEGRITY—CAN THE PHYSICIAN BE A CONSCIENTIOUS OBJECTOR IN MEDICINE?

Anesthesia care of patients can involve ethical controversy, legitimate disagreement, and moral ambiguity. How a physician resolves moral conflicts when their personal

values run counter to acceptable ethical standards of care is a matter of much concern.<sup>145,146</sup> Medical professional societies recognize the right to conscientious objection in medical practice. The ASA, the British Medical Association, and the bioethics research institute, The Hastings Center, all have issued statements recognizing the physician's right to withdraw from situations in which ethical standards of patient care are in serious conflict with his or her personal values.<sup>147</sup> The ASA specifically recognizes conscientious withdrawal from patient care in the case of patients with DNAR orders or other directives that limit treatment.<sup>25</sup> These rights have limitations, however. Acceptance of moral objections to certain hotly contended issues such as abortion or PAS may be reasonable, but objections to well-established standards, such as informed consent, are not. Moral objections of physicians are also likely to carry more weight if they involve concepts that the physician believes supports him or her as an ethical doctor, and not just as an ethical person, because these concepts are more likely to be founded in professionally established standards than in personal beliefs.<sup>147</sup> When physicians' personal religious and other moral beliefs are allowed to supersede those of patients, the result has almost uniformly been barriers in health care to vulnerable groups, such as women, adolescents, and the elderly.<sup>148,149</sup>

In early 2018, the U.S. Department of Health and Human Services moved under conservative political leadership to strengthen doctors' rights to refuse to refer patients for legal medical treatments that they personally object to, such as abortion, transgender treatments, and birth control, for example. The AMA has raised concerns that the move both combines and illegally broadens laws that have not been subjected to public vote. Dr. Lainie Friedman Ross, physician and ethicist at the University of Chicago, points out that "it is very problematic because it forgets that doctors are powerful individuals and patients are vulnerable. The law is all about protecting doctors, not the individuals who need the protection—those who are sick and frightened."<sup>150</sup> It remains to be seen whether the new rules will withstand inevitable legal challenges. In the meantime, a Canadian court ruled in the opposite direction, that the requirement to refer patients to legal medical treatments in Ontario was "a reasonable limit on the religious freedom of doctors, necessary to prevent harm and inequitable access for patients."<sup>150</sup>

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## KEY POINTS

- Mechanisms of consciousness and memory, and their interruption by general anesthetics, are important scientific problems that have clinical relevance for the practice of anesthesiology.
- Consciousness is characterized by both wakefulness (i.e., the brain being aroused) and awareness (i.e., subjective experience).
- Anesthetics act at structures in the brainstem, hypothalamus, and basal forebrain that regulate sleep-wake states, which may account for loss of wakefulness.
- Anesthetics disrupt connectivity and communication across cortical and thalamocortical networks, which may account for loss of awareness.
- Memory can be subdivided into explicit (conscious) and implicit (unconscious) recall; an example of explicit episodic recall is remembering a surgical event.
- Suppression of explicit episodic recall is one of the most potent effects of most general anesthetics.
- Effects on the hippocampus, amygdala, and prefrontal cortex—as well as the connectivity of these structures—may account for anesthetic-induced amnesia, even before loss of consciousness.

## Introduction

### SCIENTIFIC AND CLINICAL IMPORTANCE

Consciousness and memory are among the most fascinating and complex subjects in all of science. The richness of human consciousness and memory—and the ability to express this richness in language—is a defining characteristic of *homo sapiens*. Consciousness and memory also have clinical relevance for the anesthesiologist; together, the experience and explicit episodic recall of surgical events is known as the problem of “intraoperative awareness.” When formally assessed, this complication occurs in approximately 1 to 2 cases per 1000<sup>1-3</sup> and is associated with a high incidence of posttraumatic stress disorder (PTSD).<sup>4,5</sup> The incidence of intraoperative consciousness without recall is substantially higher.<sup>6</sup> To advance the field of perioperative brain monitoring, a detailed understanding of the neurobiology of consciousness, memory, and anesthesia is required.

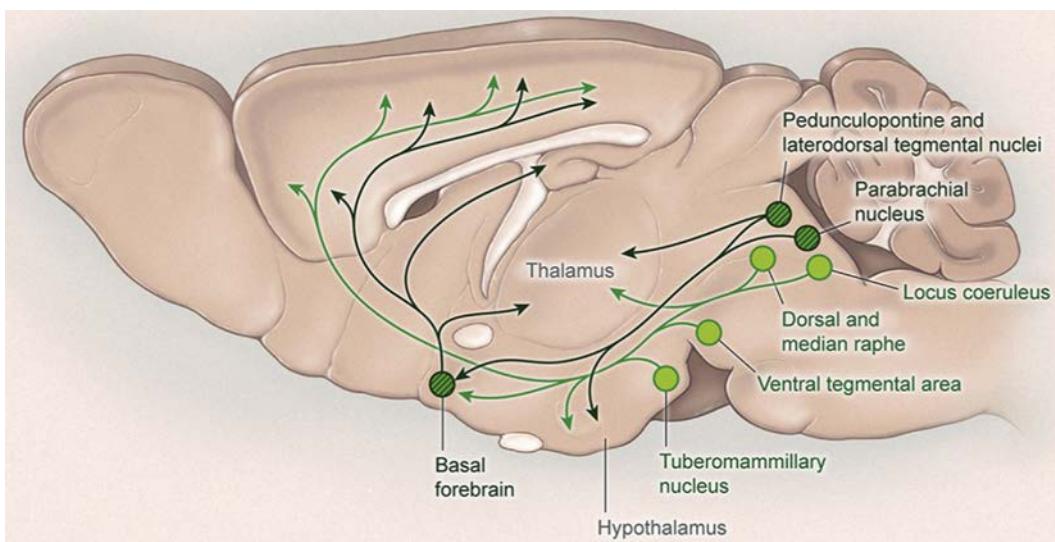
## Consciousness

### DEFINITIONS

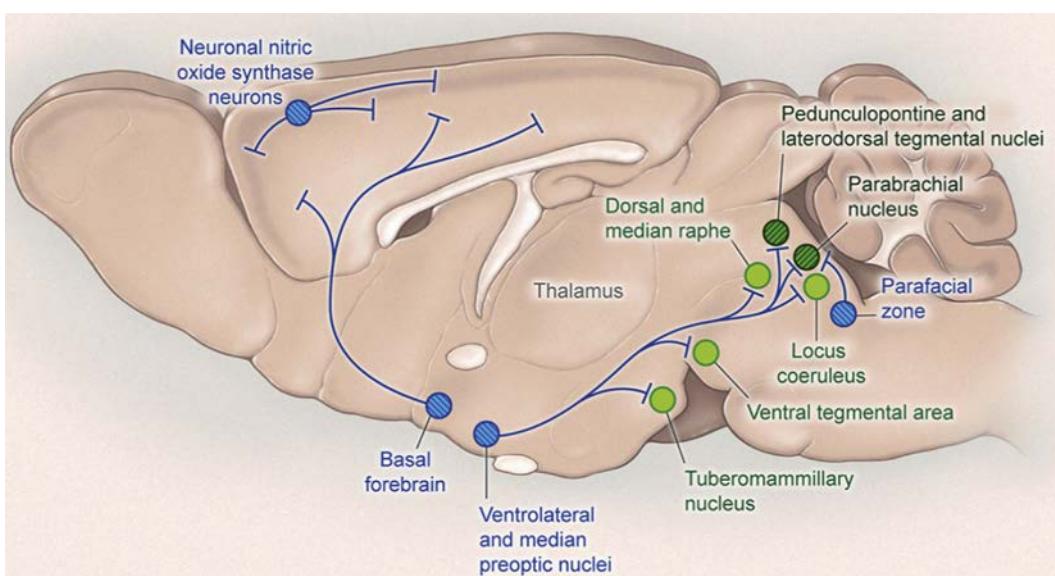
The field of consciousness studies has been plagued by the indiscriminate use of the term “consciousness.” When we refer to consciousness, we mean *subjective experience*. In simple terms, it is what we lose when we have dreamless sleep and what we regain again in the morning upon awakening. There are, however, several important definitions and distinctions that should be considered.

1. **Awareness:** Cognitive neuroscientists and philosophers use the term “awareness” to mean *only* subjective experience. In clinical anesthesiology, we (inaccurately) use the term “awareness” to include *both* consciousness and explicit episodic memory<sup>7</sup> (the taxonomy of memory will be discussed in the next major section of the chapter).
2. **Connected versus disconnected consciousness:** Connected consciousness is the experience of environmental stimuli (such as surgery), whereas disconnected consciousness is an endogenous experience (such as a dream state).<sup>8</sup>
3. **Consciousness versus responsiveness:** An individual may fully experience a stimulus (such as the command “Open your eyes!”) but not be able to respond (as when a patient is paralyzed but conscious during surgery).<sup>9</sup>

There have been a number of theories proposed to explain the mechanisms of consciousness and general anesthesia. Advances in neuroscience, however, have enabled us to move beyond speculative frameworks and focus on a systems-based approach to both subjects.<sup>10</sup> The remainder of this section on consciousness adopts such an approach by discussing (1) brainstem and hypothalamic nuclei regulating the sleep-wake cycle (and therefore arousal states) (Figs. 9.1 and 9.2); (2) the role of the thalamus in consciousness and anesthesia; (3) cortical-subcortical connectivity, with a focus on the thalamocortical system, which is thought to mediate the experiential component of consciousness; and (4) cortico-cortical communication.



**Fig. 9.1** Neurobiology of wakefulness. Multiple neurochemical systems in subcortical regions (shown here in rodent brain) promote arousal and activation of the cortex. Monoaminergic neurons (light green) in the rostral brainstem and caudal hypothalamus innervate the cortex as well as many subcortical regions including the hypothalamus and thalamus. These monoaminergic regions include noradrenergic neurons (locus coeruleus), serotonergic neurons (dorsal and median raphe nuclei), dopaminergic neurons (ventral tegmental area), and histaminergic neurons (tuberomammillary nucleus). Wake-promoting signals also arise from cholinergic regions (dark green with hatching), including the pedunculopontine and laterodorsal tegmental nuclei and basal forebrain. General anesthetics have been demonstrated to suppress many of these regions. (Redrawn from Scammell TE, Arrigoni E, Lipton JO. Neural circuitry of wakefulness and sleep. *Neuron*. 2017;93(4):747–765.)



**Fig. 9.2** Neurobiology of slow-wave sleep. GABA-ergic neurons in the ventrolateral preoptic area and median preoptic nucleus in the hypothalamus (shown here in rodent brain) promote sleep by inhibiting wake-promoting neurons in the caudal hypothalamus and brainstem. These hypothalamic nuclei are activated by general anesthetics. (Redrawn from Scammell TE, Arrigoni E, Lipton JO. Neural circuitry of wakefulness and sleep. *Neuron*. 2017;93(4):747–765.)

## SUBCORTICAL NUCLEI REGULATING AROUSAL

It was hypothesized in the mid-1990s that anesthetics suppress consciousness by actions at the subcortical nuclei that evolved to control sleep-wake cycles.<sup>11</sup> The past decades have supported the hypothesis that anesthetics interact with a number of these sleep-wake centers,<sup>12,13</sup> although precise interactions and contributions to the state of general anesthesia have yet to be elucidated. The following is a description of select subcortical nuclei in the brainstem and hypothalamus that mediate sleep-wake cycles<sup>14</sup> and, potentially, some traits of anesthesia.

## Brainstem

**Locus ceruleus.** Norepinephrine is synthesized in the locus ceruleus (LC), which is located in the pons and projects widely throughout the cortex.<sup>15</sup> Like other monoaminergic neuronal populations, LC activity is highest during waking consciousness, decreased during nonrapid eye movement (NREM) sleep, and at its nadir during rapid eye movement (REM) sleep.<sup>16,17</sup> Thus LC is associated with cortical arousal only during wakefulness and not with the cortical activation during REM sleep. LC neurons are hyperpolarized by halothane.<sup>18</sup> The role of norepinephrine (generated by LC)

in anesthesia is further supported by studies demonstrating that barbiturate anesthesia time is increased by antagonizing norepinephrine and reduced by agonizing it.<sup>19,20</sup> Norepinephrine transmission in the basal forebrain may be of particular relevance to anesthetic depth.<sup>21</sup> It has been found that LC noradrenergic neurons modulate the state of isoflurane anesthesia as well as emergence therefrom.<sup>22</sup> Of note, administration of ketamine is associated with an increase of activity in the LC<sup>23</sup> and appears to contribute to its anesthetic effects.<sup>24</sup>

LC and the role of norepinephrine in hypnosis are of particular interest due to the role of the  $\alpha$ -2 agonist dexmedetomidine in clinical care. Microinjection of dexmedetomidine in the LC results in reduced levels of consciousness that can be prevented by coadministration of the  $\alpha$ -2 antagonist atipamezole.<sup>25</sup> After exposure to dexmedetomidine, brain changes somewhat mimic NREM sleep in that the LC and tuberomammillary nucleus (TMN) are deactivated, whereas the ventrolateral preoptic nucleus (VLPO) is activated.<sup>26</sup> Data in dopamine- $\beta$ -hydroxylase knockout mice (which lack the ability to synthesize norepinephrine) demonstrate a *hypersensitivity* to dexmedetomidine, suggesting alternative mechanisms of action.<sup>27</sup> However, selective knockdown of  $\alpha$ -2A adrenergic receptors from LC prevent dexmedetomidine-induced loss of righting reflex,<sup>28</sup> a marker of general anesthesia in rodents.

**Laterodorsal/pedunculopontine tegmentum.** Along with the basal forebrain, the laterodorsal tegmentum (LDT) and pedunculopontine tegmentum (PPT) in the pons are the brain's source of acetylcholine.<sup>29</sup> There are direct projections to the thalamus from LDT/PPT with a known role in the generation of slow oscillations and sleep spindles,<sup>30</sup> which together represent a neurophysiologic sign that information transfer to the cortex is likely blocked.<sup>31</sup> As with the noradrenergic LC, activity of the LDT/PPT is high during waking consciousness and decreases during NREM sleep.<sup>15</sup> However, in contrast to the LC and other monoaminergic neurons, the cholinergic LDT/PPT is also active during REM sleep, during which the cortex is aroused. Furthermore, activation of cholinergic neurons in LDT or PPT induces REM sleep.<sup>32</sup> Thus, both states of cortical activation across the sleep-wake cycle are associated with high cholinergic tone. General anesthetics modulate cholinergic projections from the LDT/PPT. Sleep spindles occur during halothane anesthesia and are associated with decreased cholinergic transmission to the medial pontine reticular formation (PRF).<sup>33,34</sup> There is evidence that synaptic and extrasynaptic  $\gamma$ -aminobutyric acid (GABA) receptors play a role in modulating LDT neurons,<sup>35</sup> which could provide a direct link to molecular mechanisms of numerous general anesthetics. However, there has been relatively little study of the role of LDT/PPT in anesthetic mechanisms, with a greater focus on cholinergic neurons in the basal forebrain.

**Pontine reticular formation.** The PRF is part of the reticular activating system, which plays an important role in cortical arousal. Although GABA is the primary inhibitory neurotransmitter in the brain, the actions of GABA in the PRF are associated with cortical arousal.<sup>36</sup> For example, there is increased time spent in the waking state when the GABA<sub>A</sub> receptor agonist muscimol is microinjected in the

PRF.<sup>37</sup> When the GABA<sub>A</sub> antagonist bicuculline is microinjected, wakefulness is suppressed, but REM sleep (another state of cortical arousal) is triggered. Vanini and colleagues found that *decreased* levels of GABA in the PRF correlated with isoflurane-induced unconsciousness, muscular hypotonia, and decreased respiratory rate.<sup>38</sup> Since the effects of anesthetics are normally associated with a *potentiation* of GABA activity, these findings highlight that a specific neuroanatomic and neurochemical milieu can play a unique and unexpected role in the mechanisms of consciousness and anesthesia. In addition, Vanini and colleagues found that GABA-ergic transmission in the rat PRF modulates the loss of consciousness induced by isoflurane but does not appear to affect emergence,<sup>39</sup> providing evidence for asymmetry between the two processes.

The mesopontine tegmental anesthesia area is located in the PRF. When pentobarbital is microinjected in this area, a reversible state with anesthetic traits is induced.<sup>40</sup> More recently, this phenomenon has been defined with greater spatial resolution, with the identification of around 1900 neurons in this area that can induce general anesthesia.<sup>41</sup>

**Ventral tegmental area.** Dopaminergic neurons of the ventral tegmental area (VTA) in the midbrain have not classically been considered key mediators of the sleep-wake cycle because of relatively less evidence of state-dependent changes compared with neurons in other brainstem nuclei. This view has been challenged in sleep neurobiology.<sup>42</sup> A dopaminergic pathway regulating sleep-wake states has been identified in *Drosophila*.<sup>43</sup> and dopaminergic neurons of the VTA have more recently been found to play a role in mammalian sleep.<sup>44</sup> There has been renewed interest in the ability of dopaminergic activity to reverse or accelerate recovery from general anesthesia. Studies of the dopamine agonist methylphenidate have revealed an ability to reverse the sedative effects of both isoflurane and propofol.<sup>45,46</sup> VTA appears to be the source of the dopaminergic transmission mediating arousal during exposure to anesthesia, as evidenced by the fact that electrical stimulation of the VTA or selective stimulation of VTA dopaminergic neurons can reverse anesthetic-induced unconsciousness.<sup>47,48</sup>

## Hypothalamus

**Ventrolateral preoptic nucleus.** The anterior hypothalamus has long been hypothesized to play a role in sleep-wake regulation.<sup>49</sup> VLPO is a structure in this region that transmits GABA and galanin.<sup>50</sup> Neurons in VLPO are maximally active during NREM and REM sleep;<sup>51,52</sup> the median preoptic nucleus (MnPO) is also active during sleep. Of note, the activity profile of GABA-ergic neurons in VLPO correlates with sleep amount, whereas the activity of GABA-ergic neurons in MnPO correlates with homeostatic sleep pressure or propensity.<sup>53</sup> Importantly, activity of the VLPO during sleep is correlated with inhibition of other arousal centers in the brainstem and hypothalamus.<sup>51,54</sup> Given its potentially central role as a mediator of sleep, VLPO became an attractive candidate as a mediator of anesthetic-induced unconsciousness. Nelson and colleagues demonstrated activation of VLPO after systemic administration of propofol or pentothal;<sup>55</sup> recent studies have examined the mechanistic significance of these findings. Eikermann and colleagues conducted studies of rats with *chronic* lesions of

VLPO, finding that ablation of VLPO resulted in sleep deprivation (as expected) but conferred *increased sensitivity* to the effects of isoflurane.<sup>56</sup> This finding would argue against a critical role of VLPO in the mechanism of anesthesia. However, Moore and colleagues demonstrated that *acute* lesions of VLPO conferred *resistance* to the effects of isoflurane, an effect that appeared to be mediated specifically through the sleep-active neurons in VLPO.<sup>57</sup> These neurons are actually depolarized (i.e., activated) by isoflurane. Taken together, these data suggest that VLPO plays a role in anesthetic-induced unconsciousness (as evidenced by acute lesion data), but that the effects of sleep deprivation associated with chronic VLPO lesions could overwhelm this role. Curiously, direct administration of dexmedetomidine, an  $\alpha$ -2-adrenergic agonist, to the VLPO can destabilize the state of isoflurane anesthesia.<sup>58</sup>

**Orexinergic neurons.** Orexinergic neurons are found in the lateral hypothalamus and provide an important arousal stimulus for the cortex. There are two types of orexin (A and B), which are also referred to as hypocretins. Orexinergic neurons innervate other arousal centers in the brainstem and basal forebrain, and fire maximally in the waking state, are suppressed during NREM sleep, and show occasional bursts during phasic REM sleep.<sup>59,60</sup> Dysfunction of the orexinergic system is associated with narcolepsy in both human and animal models.<sup>61,62</sup> The often dramatic delay of anesthetic emergence in narcoleptic patients<sup>63</sup> has motivated the study of orexin in anesthetic mechanism. Orexins attenuate the effects of isoflurane,<sup>64</sup> propofol,<sup>65</sup> ketamine,<sup>66</sup> and barbiturates,<sup>67</sup> using various measures. Local infusion of orexin in the basal forebrain is associated with electroencephalographic (EEG) arousal and decreased emergence time in animals anesthetized with sevoflurane<sup>68</sup> and isoflurane.<sup>69</sup> Microinjection of propofol in the perifornical region of the hypothalamus (the locus of orexinergic neurons) is associated with a decrease in cortical acetylcholine, an important mediator of arousal.<sup>70</sup> Importantly, both genetic and pharmacologic studies have demonstrated that orexins play an important role in emergence from sevoflurane and isoflurane anesthesia, but not induction.<sup>71</sup> This seminal study suggested that there is a distinct neurobiology of induction and emergence, and formed the basis for a theory of “neural inertia” across state transitions.<sup>72</sup> Of note, halothane did not show an effect on orexinergic neurons and emergence time was not altered in orexin knockout mice.<sup>73</sup> These findings have been confirmed for propofol anesthesia: propofol reduces activity in orexinergic neurons in rats and infusion of orexin in the basal forebrain affects emergence time, but not induction time.<sup>74</sup> Orexins might facilitate emergence from anesthesia through actions in the basal forebrain.<sup>75</sup>

**Tuberomammillary nucleus.** The TMN is located in the caudal hypothalamus and is the brain’s source of histamine, an arousal-promoting transmitter. TMN activity and histamine levels are highest during wakefulness and lowest during sleep;<sup>76</sup> the TMN is thought to have a relationship of reciprocal inhibition with the sleep-promoting GABAergic neurons of the VLPO.<sup>51,54,77</sup> Histamine release in the anterior hypothalamus is depressed during sleep<sup>78</sup> and halothane anesthesia.<sup>79</sup> Systemic administration of propofol,

pentothal, and the GABA agonist muscimol all result in decreased activity in the TMN.<sup>55</sup> Microinjection of histamine in the nucleus basalis magnocellularis of the basal forebrain reverses the depressant effects of isoflurane on the EEG, an effect likely mediated by H1 histamine receptors.<sup>80</sup> A recent study in which GABA<sub>A</sub> receptors were genetically removed demonstrated that histaminergic neurons are resistant to the effects of propofol.<sup>81</sup> However, at the behavioral level, there was no effect of propofol on loss-of-righting reflex, a surrogate for anesthetic-induced unconsciousness. Thus the role of TMN and histaminergic transmission in the mechanism of anesthesia is still unclear.

## ROLE OF THE THALAMUS

The thalamus is composed of more than 50 nuclei and subnuclei that can be grossly classified as relays for sensory input from the periphery or multimodal, integrative regions that receive input from the cortex. Additionally, the thalamus is critical for transmitting arousal signals from the brainstem and for regulating cortical communication. The involvement of the thalamus in arousal, sensory processing, and cortical computation is likely critical for normal consciousness. As such, the thalamus has been of continued interest to those investigating mechanisms of anesthetic-induced unconsciousness.

The thalamus has been proposed as an ON/OFF switch for anesthetic state transitions.<sup>82</sup> This theory was generated based on the consistent metabolic depression of the thalamus by a number of inhaled and intravenous anesthetics<sup>83-85</sup> (with the exception of ketamine),<sup>86</sup> suggesting that it could serve as an effective OFF switch. The hyperpolarization of the thalamus would shift tonic firing to burst firing that—as with sleep—would prevent afferent sensory stimuli from arousing the cortex. Importantly, however, sensory nuclei in the thalamus (and their connectivity to the cortex) appear to be less involved in anesthetic-induced unconsciousness compared to the higher-order or “nonspecific” nuclei.<sup>87,88</sup>

Evidence for the thalamus as an ON switch has been derived primarily from animal experiments, in which stimulation of the centromedial thalamus by either nicotine or antibodies blocking voltage-gated potassium channels could reverse the effects of inhaled anesthetics.<sup>89,90</sup> Although microinjection of large doses of nicotine into the thalamus could precipitate anesthetic emergence, antagonism of nicotinic acetylcholine receptors in the same location did not appear to contribute to anesthetic-induced unconsciousness. Central thalamic activation results in behavioral improvement in humans with traumatic brain injury.<sup>91</sup> A study in humans demonstrated that (spontaneous) activation of the thalamus along with other subcortical structures is correlated with recovery from anesthesia, suggesting the involvement of the thalamus in the primitive or “core” consciousness observed at emergence.<sup>92</sup>

Nonspecific nuclei of the thalamus have been proposed as a computational blackboard for the cortex.<sup>93</sup> Thus if the mechanism of anesthetic-induced unconsciousness was achieved primarily by a suppression of cortical computation, a depressed thalamus should be the result. To address this question, Velly and colleagues conducted a neurophysiologic study using scalp EEG (reflecting cortical signals)

and subthalamic nuclei electrodes (argued to reflect thalamic activity).<sup>94</sup> Induction of anesthesia with either propofol or sevoflurane was associated with cortical rather than subcortical changes, suggesting that the depression of the thalamus identified through neuroimaging studies reflected an effect rather than a cause of anesthetic-induced unconsciousness. Other case studies in humans suggest concurrent suppression of thalamus and cortex during induction of propofol.<sup>95</sup> Furthermore, more precise neurophysiologic recordings of thalamus and cortex in animal models suggest that effects of propofol on central thalamic activity precede effects on the cortex; interestingly this was found during the spontaneous induction of sleep as well.<sup>96</sup> Other animal studies have found that attenuation of high-frequency oscillations by propofol is more pronounced in the thalamus than the cortex.<sup>97</sup>

The prior two possibilities (thalamic switch or computational blackboard for the cortex) treat the thalamus as a passive player in general anesthesia. However, more recent data suggest that it might, instead, play an active role. A computational study using human EEG data and modeling suggested that the action of propofol on GABA receptors in the nucleus reticularis generates a hypersynchronous alpha rhythm (8–13 Hz) with the frontal cortex that blocks sensory input.<sup>98</sup> Hypersynchrony of alpha may block the flexible corticocortical communication required for normal consciousness.<sup>99</sup> A recent animal study identified alpha synchronization between thalamus and medial prefrontal cortex during propofol induction.<sup>100</sup> The potential role of thalamocortical interactions in anesthetic-induced unconsciousness prompts further discussion of the thalamus and its connectivity to the cortex.

### CORTICAL-SUBCORTICAL CONNECTIVITY

The closely integrated function of the cortex and thalamus suggests that the two can be treated as a single *thalamocortical system*. The thalamocortical system undergoes state-dependent changes across the sleep-wake cycle, and is thought to play a critical role in consciousness. This role is defined by its ability to integrate the activities of functionally diverse cognitive modules, a property that is critical for subjective experience.<sup>101</sup>

Recent studies using functional magnetic resonance imaging (fMRI) have refined the role of thalamocortical connectivity in anesthesia. One study identified a propofol-induced disruption of connectivity between the thalamus and lateral frontal-parietal networks.<sup>102</sup> Similarly, a study of the specific nuclei (linked to particular sensory modalities) and nonspecific nuclei (linked to integrative functions) found that disrupted connectivity between the nonspecific nuclei and the cortex best accounted for a reduction in the level of consciousness by propofol.<sup>87</sup> Recently, the inhaled anesthetic sevoflurane has been shown to functionally disconnect the thalamus and cortex, especially frontal cortex.<sup>103,104</sup> Notably, a consistent finding of neuroimaging studies is that the thalamocortical connectivity of primary sensory networks is relatively well preserved despite anesthetic-induced unconsciousness.

The finding of impaired thalamocortical connectivity in association with anesthetic-induced unconsciousness has not been universal. An fMRI study of propofol revealed more

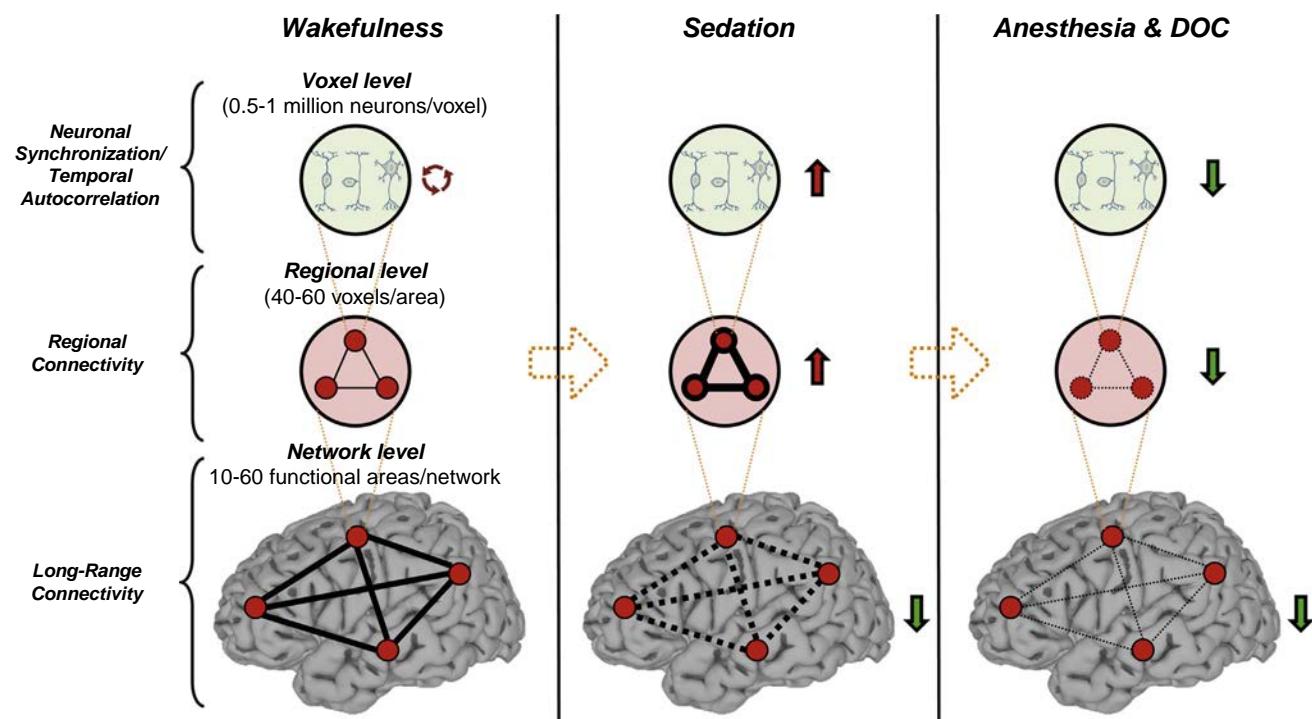
profound functional disconnections between the cortex and putamen, a subcortical structure in the basal ganglia.<sup>105</sup> In contrast, thalamic connectivity was relatively well preserved. The potential role of the striatum (composed of the putamen and caudate) in anesthetic-induced unconsciousness has been demonstrated in a study of rats undergoing isoflurane anesthesia.<sup>106</sup> This study was conducted with fMRI and found that the functional connection between the frontal cortex and the basal ganglia was disrupted during general anesthesia. A functional disconnection of association cortex and subcortical structures has also been shown by fMRI in a study of propofol-induced unconsciousness in humans.<sup>107</sup> With improved spatial resolution of 7T fMRI machines and templates for brainstem nuclei,<sup>108</sup> future studies can focus on identifying with greater precision the critical subcortical and cortical interactions or functional disconnections that contribute to anesthetic-induced unconsciousness.<sup>109</sup>

### CORTICAL CONNECTIVITY AND DYNAMICS

The last three sections were organized according to a bottom-up approach to consciousness and anesthesia, starting with the brainstem, and then moving to the diencephalon and thalamocortical system. Sleep is clearly generated through such bottom-up mechanisms<sup>14</sup>; however, anesthetics may suppress the *level* of consciousness through bottom-up mechanisms and *content* of consciousness through top-down (i.e., cortical) mechanisms.<sup>12</sup>

Early studies using positron emission tomography (PET) demonstrated regional depression in cortical areas, including lateral and medial frontal-parietal networks.<sup>110</sup> Disruption of fMRI-based functional connectivity in frontal-parietal networks has been demonstrated during anesthetic-induced unconsciousness induced by drugs with distinct molecular mechanisms, including propofol,<sup>102,111</sup> sevoflurane,<sup>103</sup> and ketamine.<sup>112</sup> However, the cortex is amenable not only to fMRI but also neurophysiological techniques of assessing connectivity, enabling data on anesthetic-induced unconsciousness with improved temporal resolution. EEG can be used to measure functional connectivity (the statistical covariation of the activities of brain regions), and directional or effective connectivity (the presumed causal influence of one brain region on another).<sup>113</sup> Using such techniques applied to EEG (in some cases with concomitant fMRI), disruption of frontal-parietal connectivity and surrogates of information exchange in humans has been consistently observed after administration of a variety of anesthetics with diverse molecular targets.<sup>104,114–117</sup> It has been suggested that such disruption of frontal-parietal connectivity, with implications for impaired information transfer of relevance to consciousness, might be a common mediator and proximate cause of anesthetic-induced unconsciousness.<sup>118</sup>

The inhibition of frontal-parietal communication is likely representative of a more global disruption of cortical communication. A study using high-density EEG and transcranial magnetic stimulation revealed an inhibition of cortical-effective connectivity after midazolam-induced unconsciousness.<sup>119</sup> After administration of the benzodiazepine, local cortical activation could be observed at the site of magnetic stimulation, but robust evoked potentials



**Fig. 9.3** Schematic summary of the consecutive stages of unconsciousness. Relative to the control state of wakefulness (left column), sedation (middle panel) is marked by an increase of local/regional signal synchrony and consequent breakdown of global connectivity. Deep surgical anesthesia or disorders of consciousness (DOC, right column) is associated with collapse of both local/regional synchrony and global connectivity. (From Huang Z, Liu X, Mashour GA, Hudetz AG. Timescales of intrinsic BOLD signal dynamics and functional connectivity in pharmacologic and neuropathologic states of unconsciousness. *J Neurosci*. 2018;38(9):2304–2317.)

were terminated at less than 100 milliseconds, and cortical communication was limited. Of note, this finding is consistent with findings in NREM sleep.<sup>120</sup> This perturbational approach determined that the complexity of cortical response to a stimulus decreased during sleep, general anesthesia, and disorders of consciousness.<sup>121</sup> The concordant findings across physiologic (sleep) and pharmacologic (anesthesia) states of unconsciousness may reflect a common neurophysiologic mechanism of disrupted cortical connectivity through slow oscillations, which share a number of characteristics in NREM sleep and general anesthesia.<sup>122</sup> A study of three epilepsy patients with intracranial neurophysiologic monitoring<sup>123</sup> revealed that, within 5 seconds of propofol-induced unconsciousness, there was a dramatic increase in the power of slow oscillations. Although single-unit neuronal activity was initially suppressed, it returned to baseline (or above baseline) but was fragmented into highly active and quiescent periods. Neural firing became coupled with the slow oscillation. However, the slow oscillations themselves demonstrated decay in phase coupling with increased distance across the cortex. Thus neuronal spike activity became fragmented into “on” and “off” periods, which became temporally uncoordinated across the cortex. These neurophysiologic conditions dramatically reduce the probability of meaningful corticocortical communication.

More recent trends of analyzing cortical changes during states of unconsciousness take a dynamic approach that reflects not just connectivity configurations but the repertoire of states that can be accessed during general anesthesia. For example, there is a contraction of dynamic repertoire and neural signal diversity during

propofol-induced unconsciousness<sup>124,125</sup> that would preclude the kind of flexibility required for normal conscious experience. Dynamic patterns are impaired during general anesthesia and cortical dynamics are stabilized during general anesthesia.<sup>126</sup> This is likely a discrete, multistage process with distinct dynamic signatures during sedation and general anesthesia (Fig. 9.3).<sup>127,128</sup> Relating dynamics to connectivity, it appears that the repertoire of functional connectivity patterns in the primate brain becomes more tethered to structural/anatomical connectivity patterns during the anesthetized state.<sup>129</sup> Of note, animal studies suggest that the return of consciousness after general anesthesia is defined by discrete neural states that reconfigure during emergence.<sup>130</sup>

In the next section, we discuss memory, the thread that links conscious experiences together to form the narrative of “self.”

## Memory

### HISTORY AND TERMINOLOGY

Modern understanding of the structure, function, and organization of human memory is deeply informed by the study of amnesia. The most renowned demonstration of this principle occurred in 1957, when Brenda Milner reported the remarkable case of Henry Gustav Molaison (1926–2008),<sup>131</sup> an amnesiac who would become known famously as H.M., and who would represent the single most influential case study in the history of neuroscience. In a procedure intended to treat a refractory seizure disorder,

significant portions of the medial temporal lobe (MTL) were removed bilaterally—including the hippocampus, amygdala, and adjacent parahippocampal gyrus. H.M. developed profound and enduring anterograde amnesia, and was unable to establish any new conscious memory, irrespective of the sensory modality. He also developed a temporally graded window of retrograde amnesia, with impaired recall of events occurring during the 3 years preceding his surgery. However, most of his associated cognitive functions—perceptual processing, language, attention, access to semantic knowledge, and capacity to retain small packages of information in constant rehearsal—remained largely or entirely intact. Prior to this report, the prevailing theory—articulated by Canadian neuropsychologist Donald Hebb<sup>132</sup>—was that there was no brain region dedicated to memory function. Instead, memory processes were thought to be distributed and integrated into region-specific perceptual and cognitive functions. For example, the visual attribute of a memory would be wholly served within the striate and extrastriate cortical regions responsible for visual perception. The description of H.M. immediately disproved this model. It became clear that the MTL was a specialized and obligatory structure for the establishment and early maintenance of *all* conscious memory, irrespective of the modality. The trajectory of memory research was profoundly transformed. Initially, largely independent branches evolved to focus on the structural-functional organization of the MTL (Fig. 9.4A) and the nature of cellular-level neuroplastic processes—the latter notably marked by the description of long-term potentiation (LTP) by Timothy Bliss and Terje Lømo in 1973.<sup>133</sup> Subsequently, emerging technologies enabled the development and investigation of systems-level constructs. Examples include the use of EEG and magnetoencephalography to assess the role of oscillatory phase synchronization in neuronal assemblies,<sup>134</sup> fMRI to identify large-scale networks associated with specific memory functions,<sup>135</sup> and machine learning to classify complex neural network patterns predictive of memory.<sup>136</sup>

Amnesia is the term used to describe one of the cardinal properties of general anesthesia. As understood by most anesthesiologists and laypeople, this description is phenomenological; it states that patients do not recall the events that occur to them while receiving anesthesia. However, this usage confuses a critical mechanistic and semantic distinction. Patients in the deepest states of anesthesia are unable to process and bind perceptual elements into an integrated conscious experience. From the perspective of cognitive neuroscience, the “amnesia” of general anesthesia is not a primary failure of memory, but rather a failure of consciousness. It simply reflects that a conscious experience cannot be reconstructed by memory processes when it does not exist in the first place. Further confusion is added by the frequent use of the term *awareness*—a synonym for conscious perception—to describe the case in which a patient consciously recalls events occurring during the administration of an anesthetic. This ignores the fundamental principle that memory is functionally dissociable from consciousness. Awareness is *necessary* for the establishment of memory under anesthesia, but it is not *sufficient*. Conscious recall can occur only if awareness is accompanied by memory processes in the MTL and elsewhere that establish and preserve a representation that can be reconstructed later.

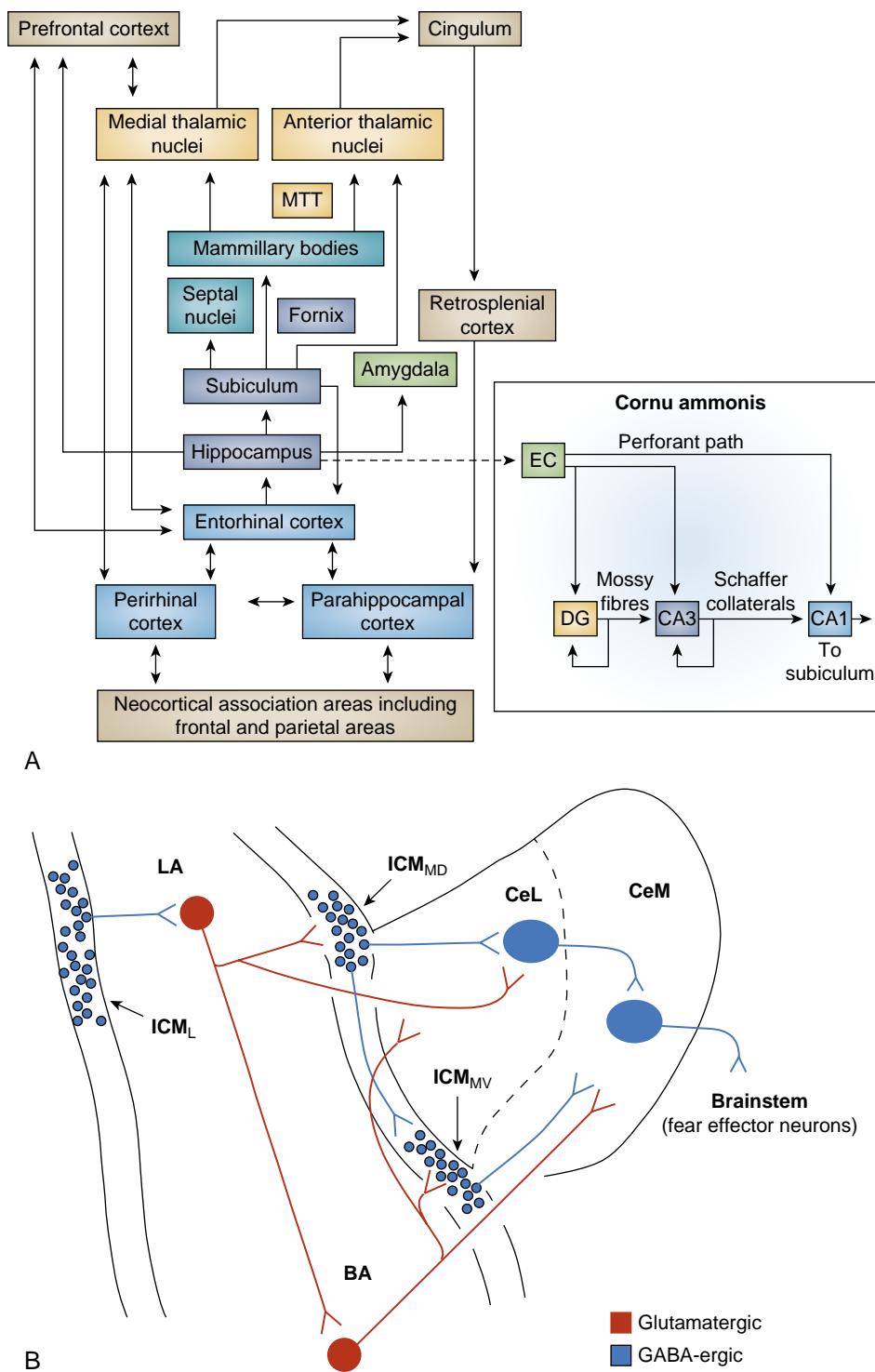
These important distinctions establish the axiom that patients who form memories while under anesthesia cannot have been truly unconscious; they must have possessed some conscious substrate from which the memory derives. However, the converse inference is not always true: the existence of consciousness will not necessarily lead to the existence of memory if an anesthetic drug is present. Evidence to support this statement is unambiguously encountered in everyday anesthetic practice—patients receiving a small dose of propofol or midazolam who engage in a cogent conversation that they are later unable to recall, or in patients emerging from general anesthesia who follow commands to demonstrate that extubation can proceed safely, yet later cannot recall anything related to this clearly conscious event. Anesthetic drugs must therefore have direct effects on memory processes that are dissociable from those on consciousness—and it is this observation that provides a framework for the systematic study of how anesthetic drugs affect memory.

## Organization and Function of Normal Memory

### MULTIPLE MEMORY SYSTEMS

When the term *memory* is used in everyday language, it almost always refers to declarative memory. Declarative memory is the representation of prior events and knowledge that is accessible to consciousness and can be manipulated by attention and executive function. It is the form of memory referred to in the context of anesthetic amnesia.

Further important organizational structure exists within declarative memory. The first is the distinction between episodic and semantic memory. *Episodic memory* is the recollection of events with a clear spatiotemporal context (as when recalling autobiographical events with a distinct sense of personal experience, time, and place), whereas *semantic memory* is the capacity to recall and apply meaning, facts, and knowledge without spatiotemporal context (as when recalling that Mount Everest is the tallest mountain in the world without any sense of time and place for the acquisition of that knowledge). The episodic memory system is fast-mapping and highly dependent on the MTL as well as frontal and parietal structures,<sup>137,138</sup> whereas the semantic memory system is slower and involves distributed cortical regions that closely map to the default mode network, a large-scale system that is active during the resting state and flow of spontaneous cognition.<sup>135,139</sup> The second organizational structure within episodic memory is the distinction between recollection and familiarity. *Recollection* involves remembering specific qualitative contextual details about a prior event, whereas in a *familiarity* judgment, there is a sense that an item has been encountered previously, but beyond that there are no added contextual details. The accepted understanding is that recollection and familiarity arise from distinct processes and neural architecture within the MTL. The perirhinal cortex receives input from sensory association areas and supports familiarity judgments through encoding and retrieval of the identifying qualities of an item (the “what” information). The parahippocampal cortex and entorhinal areas receive input from areas



**Fig. 9.4** Memory systems in the medial temporal lobe. (A) Representation of unidirectional and bidirectional network connectivity of structures in the medial temporal lobe, dienephalic nuclei, and neocortical association areas. CA, Cornu ammonis; DG, dentate gyrus; EC, entorhinal cortex; MTT, mammillothalamic tract. (B) Intrinsic connectivity of the amygdala. BA, Basal nucleus; CeL, central nucleus lateral segment; CeM, central nucleus medial segment; ICM<sub>L</sub>, lateral intercalated cell mass; ICM<sub>MD</sub>, dorsomedial intercalated cell mass; ICM<sub>MV</sub>, ventromedial intercalated cell mass; LA, lateral nucleus. ([A] Modified from Bartsch T, Butler C. Transient amnesia syndromes. *Nat Rev Neurol*. 2013;9[2]:86–97, Figure 2. [B] Modified from Duvarci S, Pare D. Amygdala microcircuits controlling learned fear. *Neuron*. 2014;82[5]:966–980, Figure 2.)

processing spatial information (the “where” information), and support recollection through encoding and retrieval of context. The hippocampus links these two, binding item and context information, and appears necessary for recollection, but plays little or no role in familiarity.<sup>140,141</sup>

Other forms of memory are dissociable from declarative memory. Findings that amnesiacs could learn a hand-eye coordination skill even while possessing no memory of the task led to the distinction between declarative and *procedural* memory, which is dependent on the caudate nucleus.

Subsequently, memory-impaired patients were also found to have intact *priming*,<sup>142</sup> which is a nonconscious process in which exposure to a stimulus influences the response to a later stimulus—for example, amnesiacs can name pictures 100 milliseconds faster if they have seen them previously, despite having no declarative memory of the exposure.<sup>143</sup> The neural bases for priming effects are thought to arise within regions serving perceptual and contextual processing of the stimulus, and so vary with the nature of the task.<sup>144</sup> Lastly, a large body of work has extensively elucidated the *emotional memory* system. The classic experimental model is Pavlovian fear conditioning and its variants, wherein an emotionally neutral conditioned stimulus is paired with an aversive unconditioned stimulus, leading to an involuntary associative physiologic and/or behavioral response to the conditioned stimulus. The circuitry involves convergence of afferent information from all sensory modalities on the lateral nucleus of the amygdala, and the basolateral and central nuclei projecting widely to modulate processes in cortical and subcortical regions (see Fig. 9. 4B).<sup>145,146</sup> With the progressive description of these and other functional distinctions, the framework for understanding memory eventually shifted to models that contained multiple memory systems in the brain, distributed functionally and anatomically.<sup>147</sup>

*Working memory* refers to the capacity to maintain limited amounts of information in the stream of consciousness, which can be manipulated to perform complex cognitive tasks such as reasoning, comprehension, and learning.<sup>148</sup> The concept evolved from, and has largely replaced, earlier ideas about *short-term memory*, but the terms should not be used interchangeably, as working memory implies both a short-term memory store *and* the capacity for manipulation. The most influential current model, first proposed by Baddeley and Hitch in 1974,<sup>149</sup> divides working memory into capacity-limited component subsystems: a *phonological loop* that maintains information through vocal or subvocal rehearsal, such as when one holds a telephone number in mind; a *visuospatial sketchpad*, which holds and manipulates spatial, visual, and kinesthetic information; and a *central executive*, which is responsible for regulating selective attention and inhibition. A fourth subsystem, the *episodic buffer*, was later added to the model<sup>150</sup> and is responsible for the temporary storage of multidimensional representations and integration with declarative memory.

Working memory has long been understood to not involve the MTL,<sup>151</sup> although the belief that it has no role has recently been questioned in studies of spatial working memory.<sup>152</sup> Notwithstanding, current understanding of working memory suggests that it is served by persistent activity and flexible resource allocation in a distributed cortical network, with a critical hub in the dorsolateral prefrontal cortex (DLPFC) interconnected with parietal cortex, thalamus, caudate, and globus pallidus.<sup>153</sup> The functional and structural distinction between working memory and the MTL does not mean that working memory and declarative memory systems do not interact. Working memory depends on declarative memory representations to provide semantic meaning and context. During working memory tasks, cortical perceptual areas associated with representations of declarative memory become activated and show increased synchrony with prefrontal regions.<sup>154</sup> Reciprocally, encoding of declarative memory is strongly influenced by the nature of processing

occurring in working memory, with deeper levels of executive processing resulting in better learning.<sup>155</sup>

The transition of memory from short-term stores through to stable long-term stores is experienced as continuous and was assumed to reflect sequential transfer across systems. However, this model is challenged by rare case examples of patients who have a selective short-term memory deficit but intact declarative memory function, and recent studies have reinforced the view that memories are formed in multiple systems in parallel.<sup>156</sup>

## LONG-TERM POTENTIATION, SYNAPTIC TAGGING, AND THE CONSOLIDATION MODEL OF MEMORY

The consolidation hypothesis of memory was first proposed by Müller and Pilzecker in 1900.<sup>157</sup> They noted that memory for new information could be disrupted by learning other information shortly after the initial training. This effect, called *retroactive interference*, is temporally graded such that the susceptibility of the memory is greatest immediately after learning and decreases with time. Müller and Pilzecker proposed that the memory trace must initially exist in a fragile state, but subsequently becomes stable through the process of *consolidation*. The consolidation hypothesis remains the framework for understanding the temporal course of memory processes and behavior.

For a memory trace to be consolidated, it must of course be created. The term used to describe this process is *encoding*. Encoding implies that the networks mediating the neural representation of an event as it is experienced do not immediately return to their previous state and are modified in such a way that potentiates reactivation of that representation. The *synaptic plasticity and memory hypothesis* states that activity-induced synaptic plasticity is both necessary and sufficient for the information storage underlying memory,<sup>158</sup> and within this framework encoding implies that some form of synaptic plasticity has been initiated. However, encoding cannot in itself assure the propagation of a memory trace. Encoding creates the potential for the formation of a long-term memory.

The minimal events that constitute the neural correlates of encoding are incompletely understood. Cellular models demonstrate that functional changes in synaptic strength can occur in the absence of any structural change in dendritic spines.<sup>159</sup> The perpetuation of these initial changes through structural and functional remodeling represents the neural correlate of memory consolidation. The prevailing cellular model for this is LTP,<sup>160</sup> which describes a durable increase in synaptic transmission efficiency following a stimulation protocol. It is now recognized that LTP occurs richly throughout the hippocampus, as well as in other afferent pathways.<sup>161</sup> LTP can be induced by nonphysiologic high-frequency stimulation, but also by stimulation protocols that resemble physiologic activity, the most important being bursts in the theta range (4–8 Hz).<sup>162</sup> This is of notable relevance to memory, as synchronized hippocampal theta oscillations appear critical to successful memory behaviors.<sup>134</sup>

The breadth and depth of literature on the mechanisms of LTP are far too voluminous to summarize here. Nonetheless, certain principles are essential and relevant to anesthesia studies and can be stated succinctly. The induction of most forms of LTP requires activation of postsynaptic N-methyl-D-aspartate (NMDA) receptors,<sup>163</sup>

followed by influx of  $\text{Na}^+$  and  $\text{Ca}^{2+}$ . This rise in intracellular  $\text{Ca}^{2+}$  is the critical trigger for LTP. Calcium-calmodulin-dependent kinase II (CaMKII) is then activated and autophosphorylated,<sup>164,165</sup> leading to cytoskeletal reconfiguration.<sup>166</sup> Activation of several other cell-signaling cascades also contribute to LTP. The terminal expression of LTP is protein synthesis, occurring in both the soma and local dendrites, and resulting in enduring structural changes at the synapse.<sup>167</sup> Protein synthesis inhibitors have been demonstrated to consistently prevent sustained LTP in vitro and learning in vivo.<sup>168</sup>

LTP thus proceeds in two phases: early LTP (E-LTP) is independent of protein synthesis and can be sustained across an interval of minutes to a short number of hours, while late LTP (L-LTP) is dependent on intracellular signaling and protein synthesis and can be sustained across many days. The *synaptic tagging and capture hypothesis* provides a mechanistic explanation for the observation that the persistence of synaptic potentiation (and memory) is influenced by events surrounding encoding.<sup>169</sup> In this model, synapses activated during E-LTP become tagged via a protein synthesis-independent mechanism. This tag establishes the potential for sustained L-LTP, but for the cascade to continue the tags must capture plasticity-related proteins (PRPs) synthesized in the soma or dendrites in response to neural activity. The synaptic tagging model explains how the thousands of dendrites of a single neuron can be engaged in memory stabilization processes in various states of evolution, because the tagging and PRP capture need not occur as a singular event.

## RECONSOLIDATION

A major shift in understanding of consolidation occurred in 2000, when Nader et al. reported that an old memory for auditory fear conditioning, which would normally not be sensitive to protein inhibitors, can be made newly sensitive if it is retrieved.<sup>170</sup> The implication is that retrieval of a memory renders it transiently plastic, after which it restabilizes. This process is termed *reconsolidation*, and the period of plasticity is termed the *reconsolidation window*. The mechanism shares many of the LTP processes that are associated with initial consolidation, but also has features that are quite distinct at both the cellular and systems level.<sup>171</sup> Reconsolidation serves as a modulatory process that enables the strengthening of an existing memory, but it is also clear that it provides a window within which an existing memory is malleable and can be updated with the addition of novel information, or diminished through interruption of restabilization processes.<sup>172</sup> These latter properties have generated significant translational interest because of repeated demonstrations of the ability to modify or even eliminate fear memory in animals through pharmacologic and behavioral interventions that interrupt reconsolidation.<sup>173</sup> Indeed, the erasure of fear memory in humans can be demonstrated through performance of a behavioral extinction procedure during the reconsolidation window.<sup>174</sup>

## PHASE SYNCHRONIZATION AND COUPLING

The neurons in assemblies and networks undergo oscillatory activation and inhibition. Phase synchronization of

these oscillations supports neural communication by creating transient and dynamic associations between different functional brain regions. Phase synchronization appears to be fundamental to neural plasticity and memory,<sup>134</sup> and numerous studies have demonstrated that dynamics of synchrony during memory tasks can be related to both long-term<sup>175</sup> and working memory<sup>176</sup> performance. Gamma-band (30-100 Hz) synchrony is believed to support an important form of Hebbian plasticity, termed spike-timing-dependent plasticity, in the hippocampus. Both computational models and experimental data provide evidence that rapid changes in the frequency and phase of gamma rhythms modulate this form of plasticity through coordination of presynaptic spikes in assemblies of neurons, effectively classifying which assemblies are interpreted as a single event.<sup>177</sup>

Another property of relevance to memory coding is the coupling of gamma oscillations to the phase of slower, synchronized oscillations within the theta-band (4-8 Hz).<sup>178</sup> Theta oscillations, which are prominent in the hippocampus and entorhinal cortex, undergo phase resetting in response to a stimulus. The phase reset involves widely distributed regions, and is thought to serve as an efficient mechanism for the optimization of interregional communication.<sup>179</sup> Theta phase resetting and synchrony in the hippocampal-entorhinal system are implicated in declarative memory,<sup>180</sup> and in the amygdala-hippocampal system in fear-based memory.<sup>181</sup> Coupling between theta phase and gamma amplitude is connected to declarative memory formation,<sup>180,182</sup> and, in an elegant model, is proposed to form a code for representing multiple items and spatial representations in an ordered way.<sup>183</sup> Coupling between theta phase and gamma phase enables a more precise temporal coordination of neuronal spikes, and may code for separated representations of multiple items in working memory.<sup>184</sup>

## Effects of Anesthetic Drugs on Declarative Memory Function in Humans

There are multiple potential pathways by which anesthetic drugs could interfere with memory and cause amnesia. Most of these cannot be directly assessed in humans, but the plausibility of candidate mechanisms can be indirectly examined by designing experiments that are informed by the characteristics of known memory processes. Studies of anesthetic effects on memory are most informative when conceptualized and designed with reference to robust methods and findings taken from the larger body of memory research.

## BEHAVIORAL STUDIES OF RETROGRADE MEMORY EFFECTS

Notwithstanding some isolated case reports, systematic investigations have found no evidence that anesthetic drugs cause retrograde amnesia in humans. There is no retrograde amnesia associated with induction doses of thiopental,<sup>185</sup> methohexitol,<sup>185</sup> or propofol.<sup>186</sup> Adult patients have normal memory for visual stimuli presented 4 minutes before administration of midazolam at doses of 2, 5, and 10 mg.<sup>187</sup> Similarly, memory is

normal for word lists learned in the preoperative holding area or operating room immediately before induction.<sup>188</sup> Studies in pediatric patients have shown normal memory for pictures presented immediately before sedation with midazolam,<sup>189</sup> propofol,<sup>190</sup> and dexmedetomidine.<sup>191</sup> In controlled laboratory settings using human volunteers and target-controlled infusions, studies have found no impairment of memory for pictures<sup>192</sup> or words<sup>193,194</sup> presented before sedative infusions of propofol, midazolam, thiopental, or dexmedetomidine.

There is some evidence from controlled studies that anesthetic drugs may instead lead to the opposite effect, in which memory for material presented prior to drug administration is enhanced—a phenomenon termed *retrograde facilitation*. In one study using a mildly sedative dose of propofol,<sup>195</sup> memory for words learned immediately prior to drug administration was enhanced throughout the testing period of 24 hours. Similar effects are described for midazolam and other benzodiazepines in the psychopharmacology literature.<sup>196</sup> The mechanistic explanation for retrograde facilitation can be framed by an understanding of *retrograde interference*—the observation that mental exertion inhibits the consolidation of recently formed memories, with the newest memories being most vulnerable.<sup>197</sup> The induction of new LTP interferes with recently formed LTP and memory performance, even when the tasks are unrelated.<sup>198</sup> However, when the induction of new LTP is blocked by administration of a selective NMDA antagonist after learning, interference with recently formed LTP does not occur, and memory performance improves.<sup>199,200</sup> A parsimonious explanation for the retrograde facilitation seen with propofol and benzodiazepines is that they similarly modulate the induction of new LTP via a GABA-ergic pathway, freeing consolidation resources that enhance survival of recently formed memory.

The findings of retrograde facilitation and absence of retrograde amnesia are suggestive that the key mechanisms of GABA-ergic anesthetic amnesia, at least in humans, involve very early processes in the consolidation cascade. It is more difficult to rationalize that downstream sequences represent principal targets. Were this the case, the expected effect would be interference with ongoing consolidation of memory for events occurring in the past, creating a window of retrograde amnesia. Nonetheless, an alternate model to the induction hypothesis suggests that GABA-ergic anesthetics exert a direct effect on downstream protein transcription processes,<sup>201</sup> based on evidence from rodent studies.<sup>202</sup>

The absence of pharmacologic retrograde amnesia does not dismiss the repeated finding that, in the clinical setting, a percentage of patients will not recall the immediate preanesthetic period—an effect that increases with age.<sup>203</sup> Although not systematically studied, the complex noradrenergic-mediated effects of acute stress and anxiety on memory may be contributory.<sup>204</sup>

## MATHEMATICAL MODELING OF ANESTHETIC AMNESIA

Mathematical modeling of memory decay has been used to characterize the amnestic effects of multiple intravenous anesthetic drugs,<sup>193</sup> which are accurately described by a two-parameter power decay function:

$$m_t = \lambda t^{-\psi}$$

where  $\lambda$  reflects the initial memory strength (an index of encoding), and  $\psi$  expresses the rate of decay (an index of consolidation). The drugs are characterized by marked differences in the way they modulate the two coefficients. Propofol is an archetypal amnestic drug—it permits robust encoding of material, but the information undergoes accelerated decay because of a failure of consolidation. In contrast, dexmedetomidine archetypally causes memory impairment because of a failure of information to be strongly encoded but has little or no effect on the subsequent consolidation of memories that are encoded. The benzodiazepine midazolam behaves like propofol at lower doses—selectively causing consolidation failure while leaving encoding intact—but with increasing dose a significant encoding impairment emerges. Thiopental in contrast causes marked encoding failure but demonstrates minimal effect on consolidation. The discrepant patterns observed imply that nonspecific GABA<sub>A</sub> agonism is not per se sufficient to explain the ability of a drug to cause consolidation failure.

## ANESTHETIC EFFECTS ON ATTENTION AND AROUSAL AS MODULATORS OF ENCODING

The effect of anesthetic drugs on encoding processes is related to the modulation of attention. Selective attention is governed by distinct networks mediating alertness, target orientation, and executive control<sup>205</sup>; involves modulation of neuronal phase synchrony across short- and long-range connections<sup>206</sup>; and is necessary for the successful establishment of declarative memory.<sup>207</sup> The dominant effect of most anesthetic drugs on attention is decreased arousal, with the notable exception being the NMDA antagonist ketamine, which has dominant effects on orienting and selection.<sup>208</sup> Thiopental mimics the effect of an attentional challenge task in decreasing activation in the left inferior prefrontal cortex (LIPFC), an effect that is not seen with propofol.<sup>209</sup> When tested at 225 minutes, arousal is predictive of memory for thiopental and dexmedetomidine, while propofol causes a significantly greater loss of memory than would be predicted by modulation of arousal alone.<sup>194</sup> In mathematical modeling of anesthetic amnesia,<sup>193</sup> arousal predicts the coefficient of encoding strength with precision for a range of sedative concentrations of dexmedetomidine, thiopental, midazolam, and propofol. In sum, arousal is predictive of subsequent memory for drugs that impair memory dominantly through causing encoding failure.

## NEUROIMAGING STUDIES OF CORTICAL ENCODING PROCESSES

A limited number of functional neuroimaging studies have evaluated the effect of anesthetics on cortical regional activation during memory encoding. An early PET study investigating sedative doses of propofol using a word memory task<sup>210</sup> identified that activation in LIPFC—a region associated with encoding and subsequent memory for language tasks—was conserved, suggesting that propofol did not block the processes required to support successful encoding. In contrast, activation in DLPFC—a region most associated with executive control functions and cognitive control of motor planning<sup>211</sup>—was decreased. In a subsequent investigation using an auditory depth of processing task, activation

of LIPFC was found to be decreased by sedative doses of thiopental, but again was relatively unaffected by propofol.<sup>209</sup> However, other studies have identified decreased activation in encoding areas. An fMRI study of sentence comprehension during light sedation with propofol found that decreased memory for sentences was related to decreased activation in the left inferior frontal gyrus (LIFG, within the LIPFC) and the middle temporal gyrus.<sup>212</sup> Another study using a single-word encoding task showed decreased activation in LIFG at levels of propofol sedation causing memory loss, but also found intact connectivity between LIFG and a number of frontoparietal and temporal regions associated with verbal processing and memory tasks, including the middle temporal gyrus and precuneus.<sup>213</sup>

Some functional neuroimaging studies have used experimental tasks similar to memory encoding tasks while evaluating sedative doses of anesthetic drugs, but have not assessed memory encoding as a primary aim; these are informative, but must be interpreted with caution. An early PET study of sedative doses of midazolam using a tone detection paradigm reported a dose-dependent activation decrease in Brodmann areas 9, 10, and 46, which overlap regions of both DLPFC and LIPFC.<sup>214</sup> An fMRI study of semantic word processing during propofol sedation found a dose-dependent decrease in activation of the LIFG, despite intact behavioral responses.<sup>215</sup> An fMRI study of low-dose dexmedetomidine reported a generalized suppression of bilateral prefrontal activation in Brodmann areas 9 and 10 during an emotional picture memory task, but encoding performance was not specifically analyzed.<sup>216</sup> A recent study using music stimuli found decreased activation in primary and secondary auditory processing areas at sedative doses of dexmedetomidine and midazolam, but not with propofol.<sup>217</sup> Other neuroimaging studies evaluating resting state networks, or passive activation in response to stimuli at nonresponsive levels of sedation, should not be viewed as memory experiments.

### Neuroimaging Studies of Medial Temporal Lobe Function

Two methodologically similar studies used event-related fMRI to evaluate MTL activation during low-dose infusions of propofol and dexmedetomidine. The degree of amnesia caused by propofol can be linearly related to decreased activation in the hippocampus bilaterally,<sup>218</sup> an effect that behaviorally corresponded to a failure of consolidation processes. In contrast, dexmedetomidine does not reduce the overall level of hippocampal activity, but the subsequent memory effect is attenuated, and dynamics of hippocampal activation are less predictive of subsequent memory<sup>216</sup>; one interpretation is that this reflects a downstream effect from weakened cortical encoding processes. An earlier study of the benzodiazepine lorazepam and the cholinergic antagonist scopolamine found decreased memory to be correlated with decreased activation in the anterior hippocampus,<sup>219</sup> accompanied by decreased activation in the encoding-related regions in the fusiform gyrus and inferior frontal cortex. In a largely exploratory investigation, 0.25% sevoflurane was found to reduce hippocampal activation in response to auditory and visual stimuli, but no memory performance was assessed.<sup>220</sup>

A few studies have evaluated anesthetic effects using electrocorticography and depth electrodes implanted

in epileptic patients, but none have been dedicated to memory function. One notable study evaluated the effects of mildly sedative concentrations of propofol on hippocampal spectral coherence and power characteristics at rest.<sup>221</sup> The main finding was a significant increase in hippocampal-rhinal spontaneous coherence in the delta-band, but minimal changes in other bands; cortico-hippocampal coherence was not assessed.

### STUDIES OF CORTICAL EVENT-RELATED POTENTIALS

A number of memory-dedicated studies have used the event-related potential (ERP)—a small but stereotypic positive and negative signal fluctuation in the EEG time-locked to a stimulus, and which can be isolated through summation over multiple (usually at least 50) identical trials. ERPs are thought to emerge not because new oscillations are induced, but because of a stimulus-induced phase resetting of ongoing oscillations.<sup>222</sup>

An early ERP study<sup>223</sup> of scopolamine, lorazepam, and diphenhydramine suggested that drug-induced effects on arousal and memory may be electrophysiologically dissociable, although memory was not assessed directly. Changes in the P1N1 and N1P2 early complexes, associated with arousal, were seen for all three drugs. However, changes in later complexes associated with memory, notably the P3 and N2P3, were seen only with scopolamine and lorazepam, and not with diphenhydramine, an antihistamine that causes sedation but not amnesia. This work is extended by a series of studies evaluating intravenous anesthetics and using memory-specific experimental paradigms. In a verbal memory task, propofol amnesia was associated with decreased P300 amplitude at the time of the encoding task.<sup>224</sup> In a subsequent study in which multiple drugs were carefully dosed to equivalent levels of sedation,<sup>225</sup> the true amnestic drugs with memory effects independent of sedation—propofol and midazolam—caused decreased amplitude in the P300 and N2P3 components, with the latter being the best predictor of subsequent memory performance. Across all drugs studied, the N2 latency was related to reaction time, a surrogate measure of sedation.

Another study examined early- and mid-latency ERPs originating from the midline parietal precuneal region (Pz), and related them to coefficients describing the extent of encoding and consolidation failure.<sup>226</sup> Across drugs from multiple classes and at multiple doses, consolidation failure was closely correlated with the P2 amplitude and N2 latency observed at the time of encoding. As the visual P2N2 complex is known to originate from synchronous theta oscillations,<sup>227</sup> one possibility is that a common mechanism underlying the effect of anesthetic drugs on consolidation involves changes in theta oscillations across a distributed cortico-hippocampal network occurring at the time of consolidation induction. Further, the P2N2 and memory decay coefficient were also closely correlated with reaction time, which can be related to interregional synchrony.<sup>228</sup> Unfortunately, no direct measures of cortico-hippocampal theta synchrony have yet been performed in studies of pharmacologic amnesia. Another analysis<sup>229</sup> examined the *old-new effect*, a robust phenomenon in the parietal ERP that distinguishes the response to initial item

exposure from subsequent exposures as a marker of memory strength. Propofol and midazolam caused a significant decrease in the old-new effect at 27 seconds, even though memory performance was maintained, demonstrating again an early marker of impaired memory processes that precedes behavioral detection.

Studies using very different experimental paradigms have evaluated auditory ERPs at multiple concentrations of propofol.<sup>230,231</sup> Propofol causes a dose-dependent decrease in mismatch negativity and early right anterior negativity, which are elicited in response to specific music signatures and are known to relate to associative memory operations. In contrast, the P1 complex, which derives from primary auditory processing, is not affected even at deep levels of sedation.

## Nonhuman Studies of Anesthetic Effects on Memory Processes and Behavior in the Medial Temporal Lobe

### ANESTHETIC EFFECTS ON MEDIAL TEMPORAL LOBE PLASTICITY

GABA-ergic interneurons project within and across subregions of the hippocampus,<sup>232</sup> providing an abundant density of possible targets for anesthetic drugs. In an early study using tetanic stimulation of the Schaffer collateral-commissural pathway,<sup>233</sup> isoflurane blocked the induction of LTP, and long-term depression (LTD) by low-frequency stimulation. These effects were reversed by the addition of the GABA<sub>A</sub> receptor antagonist picrotoxin, providing strong evidence that the effect of isoflurane on LTP is GABA-ergically mediated. In a similar protocol, amnestic concentrations of sevoflurane caused a failure of LTP which was prevented by the addition of the GABA<sub>A</sub> antagonist bicuculline.<sup>234</sup> A recent study of sevoflurane exposure in neonatal rats found reduced spine density of apical dendrites, synaptic ultrastructure damage, elevated expression of synaptic vesicle-associated proteins, and inhibition of LTP but not LTD.<sup>235</sup> One study of isoflurane, in which the hippocampus was studied 24 hours following anesthetic exposure, somewhat unexpectedly found improvement in cognitive performance, accompanied by evidence of upregulation of the 2B subunit of the NMDA receptor and enhanced LTP.<sup>236</sup>

A series of investigations have demonstrated that propofol inhibits the induction, but not the maintenance, of LTP, and has no effect on LTD. The effect is blocked by the addition of picrotoxin, implicating a GABA<sub>A</sub> receptor-mediated mechanism.<sup>237,238</sup> Notably, one study found that propofol inhibited LTP only at anesthetic, and not at amnestic concentrations.<sup>238</sup> Propofol has also been demonstrated to inhibit a number of component subprocesses of LTP.<sup>239-241</sup> Propofol reduces expression of activity-related cytoskeleton-associated protein (Arc) in the hippocampus in response to inhibitory avoidance training but does not appear to reduce Arc mRNA,<sup>202</sup> which is notable because it suggests a post-transcriptional mechanism.

The hippocampal GABA<sub>A</sub>ergic interneuron population is notable for a high density of the  $\alpha_5$ -subunit subtype. Of known significance to memory function, the  $\alpha_5$ -GABA<sub>A</sub>

receptor regulates the induction of LTP in response to a narrow range of frequencies in the theta range.<sup>242</sup> These observations have driven a series of anesthesia studies using  $\alpha_5$ -GABA<sub>A</sub>-knockout mice. Etomidate blocks LTP measured in CA1 neurons in wild-type mice, but not in  $\alpha_5$   $-/-$  mutants, and behaviorally the  $\alpha_5$   $-/-$  mutants are resistant to the amnestic effects of etomidate, but not to its general anesthetic effects.<sup>243</sup> Further, the effects of etomidate on LTP and memory behaviors are reversed by the addition of L-655,708, which selectively reduces the activity of  $\alpha_5$ -GABA<sub>A</sub> receptors.<sup>244</sup> The behavioral findings were later replicated with exposure to 1 MAC of isoflurane, with memory deficits observed in wild-type mice, but not in  $\alpha_5$   $-/-$  mutants or in wild types receiving L-655,708.<sup>245,246</sup> The increase in  $\alpha_5$ -GABA<sub>A</sub> receptors caused by etomidate and isoflurane does not return to baseline for at least 1 week.<sup>247</sup>

The  $\alpha_5$ -subunit subtype is not exclusive in its association with amnesia.  $\alpha_4$ -GABA<sub>A</sub> receptors are concentrated in the dentate gyrus and dorsal thalamus, and  $\alpha_4$  knockouts are resistant to the amnestic effects of isoflurane but not to its general anesthetic effects.<sup>248</sup> More equivocally,  $\beta_3$ -GABA<sub>A</sub> receptor knockout mice have been reported to be resistant to the amnestic effects of isoflurane,<sup>249</sup> while in a study using  $\beta_3$ -GABA<sub>A</sub> receptor knock-in mutants, the  $\beta_3$  subtype was not significantly associated with amnesia.<sup>250</sup> Similar equivocality has been found in studies of the  $\alpha_1$  subtype.<sup>251,252</sup>

The effects of anesthetics on hippocampal theta oscillations *in vivo* have been studied. One study used a fear-conditioning paradigm to examine amnestic concentration of isoflurane, nitrous oxide, and halothane, and reported that suppression of hippocampal-dependent contextual conditioning was proportionate to slowing of theta peak frequency.<sup>253</sup> Another study also demonstrated that isoflurane caused slowing of theta oscillations in the CA1 neuronal bundle without changing absolute power,<sup>254</sup> while in contrast the nonimmobilizer F6, which causes amnesia without sedation or a loss of motor activity, caused a loss of theta oscillatory power without slowing. Scopolamine causes amnesia at doses associated with acceleration of theta oscillations, which might otherwise be expected to improve learning.<sup>255</sup> However, a significant loss of absolute power is also observed. Together these findings suggest that individual anesthetics may cause amnesia through distinct forms of hippocampal theta disruption.

## Human and Nonhuman Studies of Anesthetic Effects on Fear Memory Systems

### THE AMYGDALA-DEPENDENT FEAR SYSTEM

The amygdala is a cluster of interconnected nuclei sitting immediately anterior to the hippocampus, with afferent and efferent projections to a wide distribution of cortical and subcortical structures. It is critical to fear learning and memory, and the systematic study of amygdala-dependent classical (Pavlovian) fear conditioning has produced much information regarding the mechanisms and circuitry.<sup>145,146</sup> The basolateral nucleus of the amygdala (BLA) also modulates the encoding and consolidation of memory in the

hippocampus and elsewhere in response to emotion, arousal, and stress.<sup>256</sup> The mechanism is dependent on noradrenergic projections terminating on both  $\alpha$  and  $\beta$  receptors within the BLA,<sup>257</sup> and can be triggered by systemic stress mediators—notably glucocorticoids<sup>258</sup> and epinephrine.<sup>259</sup> Amygdalo-hippocampal connectivity occurs via direct and indirect projections, and is dependent on theta oscillatory synchrony.<sup>181,260</sup> The amygdala contains a number of rational targets for GABA-ergic anesthetic drugs.

### STUDIES OF ANESTHETIC EFFECTS ON FEAR SYSTEMS IN NONHUMANS

As various forms of fear conditioning represent the dominant experimental method for studying memory in animal models, almost all studies of anesthetic effects on memory offer some insight into their effects on fear systems. Beyond the central conclusion from this sizeable body of literature that GABA-ergic anesthetics in general impair the acquisition of fear memory, a subset of studies are notable for their specific focus on fear circuitry and behavior.

There is substantial evidence that anesthetic effects on fear memory are mediated by GABA-ergic mechanisms in the amygdala. Selective injection of the BLA with midazolam blocks acquisition and stress enhancement of fear memory,<sup>261</sup> while lesions of the BLA block anterograde amnesia for an inhibitory avoidance task in rats receiving diazepam,<sup>262</sup> propofol,<sup>263</sup> and sevoflurane.<sup>264</sup> Further, injection of the BLA with the selective GABA<sub>A</sub> antagonist bicuculline blocks the effect of propofol<sup>202</sup> and midazolam.<sup>265</sup>

There are certain conditions under which anesthetic drugs can enhance fear memory. When propofol or ketamine is given immediately following conditioning, retention is enhanced,<sup>266,267</sup> which may represent a form of retrograde facilitation as described earlier, but retention is reduced when dexmedetomidine is similarly administered. In a rat model of PTSD, propofol and ketamine administered immediately after fear learning enhances long-term fear behavior, while dexmedetomidine has a neutral effect.<sup>267</sup> Midazolam given during extinction training, which normally inhibits learned fear expression, blocks the effect of extinction,<sup>261</sup> and also blocks fear-reducing effects when given during preconditioning contextual learning.<sup>268</sup> When sevoflurane is administered at a very low, nonsedating dose (0.11%), fear conditioning is enhanced.<sup>269,270</sup>

### STUDIES OF ANESTHETIC EFFECTS ON FEAR SYSTEMS IN HUMANS

Three functional neuroimaging studies have directly addressed anesthetic effects on emotional memory. A study using PET and path analysis (Fig. 9.5 lower panel)<sup>271</sup> demonstrated that the superior memorability that negatively arousing emotional items have over neutral items was unaffected by 0.1% and 0.2% sevoflurane, but lost at 0.25%, and was associated with decreased effective connectivity projecting from the right amygdala to hippocampus, and also from the right nucleus basalis to hippocampus. Further, sevoflurane modulated emotional perception such that items were rated more neutrally. An fMRI study demonstrated that sedative doses of propofol do not reduce activation of the amygdala in response to negatively arousing items, but activation of the

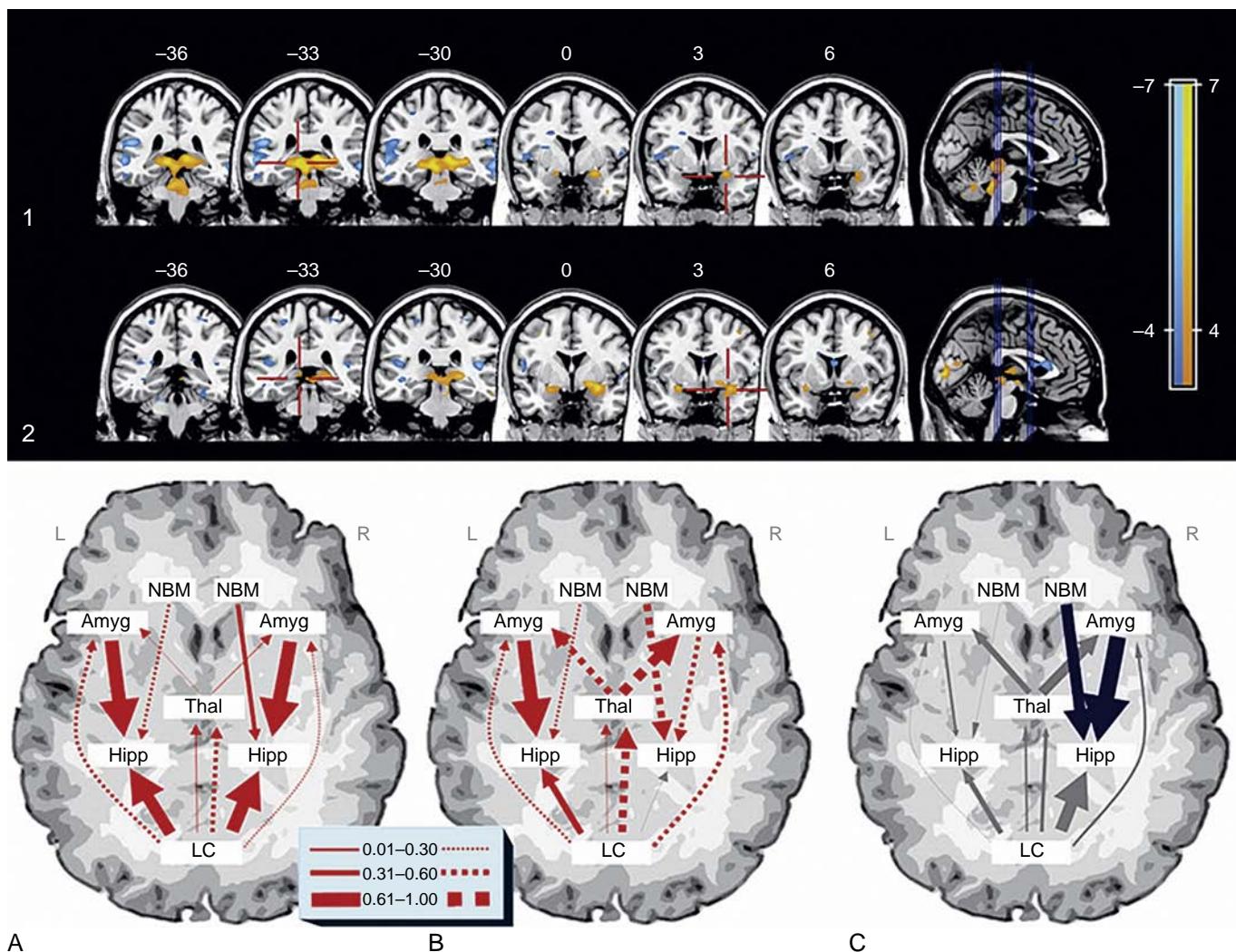
hippocampus is markedly attenuated (see Fig. 9.5 upper panel) and correlates with amnesia and loss of the superior memorability of emotional material.<sup>218</sup> This suggests that cortical and subcortical processes serving emotional interpretative functions and afferent amygdala activation are relatively spared by amnestic levels of propofol, while efferent processes underlying amygdala-dependent modulation of hippocampal plasticity are interrupted. An fMRI study of dexmedetomidine also reported no effect on activation of the amygdala in response to negatively arousing items,<sup>216</sup> but in contrast to propofol, emotional items retained superior memorability, and activation in the left amygdala and hippocampus were correlated with subsequent memory. Taken together, these studies imply that propofol may have a more targeted effect on the amygdalo-hippocampal modulatory axis. One potential explanation is that amygdalo-hippocampal connectivity is markedly interrupted by a loss of theta oscillatory synchrony caused by propofol, whereas  $\alpha_{2A}$  antagonism at the LC causes only limited downstream attenuation of noradrenergic signaling in the BLA.

### CLINICAL RELEVANCE

Amygdala reactivity is of importance in a number of fear-based psychopathologies, including anxiety, phobia, panic disorder, and PTSD.<sup>272</sup> The neurohumoral stress response to surgery and critical illness can cause complex changes in levels of catecholamines, glucocorticoids, and other potential promoters of plasticity in amygdala-dependent fear processes, occurring within a context that frequently contains emotional stressors. It is unclear under what specific conditions elevated (or depressed) levels of these mediators might contribute to long-term changes in neuropsychological functioning, although multiple studies in the critical care setting relate stress exposure, and exogenous administration of catecholamines, to negative long-term outcomes.<sup>273</sup> In a broad surgical population, the incidence of PTSD-complex symptoms related to surgery was reported to be 16%<sup>5</sup>—similar to that observed in victims of violence. The effect—or lack of effect—of anesthetic drugs on plasticity processes in the perioperative or critical care setting thus has a theoretical potential to impact long-term psychological sequelae, both positively and negatively. However, there is presently insufficient human data to inform specific recommendations.

## Anesthetic Effects on Implicit Memory Function

Implicit (nondeclarative) memory processes do not axiomatically require a conscious substrate, and are not dependent on classic hippocampal plasticity. Therefore the effect of anesthetic drugs on implicit memory functions may have important distinction from those on declarative memory, and accordingly a number of investigations have sought evidence for implicit processing in unconscious subjects. Many studies have used auditory adaptations of the *word stem completion task*, or the more rigorous *process dissociation procedure*, in which subjects are asked to exclude items that have been presented; declarative memory will drive avoidance of the target word, while implicit memory will lead to a familiarity response favoring the target word.



**Fig. 9.5** Anesthetic effects on emotional memory systems. (upper panel) Functional magnetic resonance imaging scans showing the contrast in response to negatively arousing items relative to neutral items, with coronal slices through the amygdala (0, 3, 6) and hippocampus (-30, -33, -36). The control condition (top row) shows enhanced activation of both the amygdala and hippocampus in response to the added emotional information, while in subjects receiving propofol (bottom row) there is enhanced activation of the amygdala, but not of the hippocampus. (lower panel) Path diagrams of connectivity at rest, with positive influences of one region onto another shown as solid lines, negative influences shown as dotted lines, and width representing magnitude. In the control condition (A) there is a significant positive influence of the amygdala onto the hippocampus bilaterally. Administration of sevoflurane 0.25% (B) blocks emotional modulation behaviorally, and removes the positive influence of the right amygdala and nucleus basalis of Meynert on the hippocampus. Numerical differences in path weight (C) show these two paths to significantly contribute to the network model more in the control than sevoflurane state. Amyg, Amygdala; Hipp, hippocampus; LC, locus ceruleus; NBM, nucleus basalis of Meynert; Thal, thalamus. ([A] Modified from Pryor KO, Root JC, Mehta M, et al. Effect of propofol on the medial temporal lobe emotional memory system: a functional magnetic resonance imaging study in human subjects. *Br J Anaesth.* 2015;115[Suppl 1]:i104–i113, Figure 3; [B] Modified from Alkire MT, Gruber R, Miller J, et al. Neuroimaging analysis of anesthetic gas that blocks human emotional memory. *Proc Natl Acad Sci U S A.* 2008;105[5]:1722–1727, Figure 5.)

Two early studies in patients undergoing coronary artery<sup>274</sup> and gynecologic<sup>275</sup> procedures showed evidence of implicit learning using word stem completion tasks. Another early study demonstrating implicit recall in cardiac surgery patients correlated performance with preservation of the midlatency auditory evoked potential, and most strongly with the early cortical Pa and Na complexes.<sup>276</sup> Later studies demonstrated implicit memory in both trauma patients<sup>277</sup> and patients undergoing an emergency cesarean section<sup>278</sup> using the process dissociation procedure, and further demonstrated that the degree of processing is related to the bispectral index. However, multiple more recent studies using similar procedures have either

failed to show significant implicit priming effects or have been equivocal.<sup>279–281</sup> Synthesis of these disparate results into a cohesive conclusion is difficult. Although differences in patient populations and anesthetic regimens may be of relevance, methodological challenges may have driven both false positive and false negative results. Investigations evaluating implicit memory processes in pediatric patients under anesthesia have also offered conflicting results. One study reported an increased ability to distinguish a primed animal sound from white noise,<sup>282</sup> but other investigations found no evidence of priming.<sup>283–285</sup>