Advances in minimally invasive procedures have dramatically influenced the “art of anesthesia” and will continue to do so in the years ahead. Patients and surgeons have come to expect fast-track practices that ensure comfort while minimizing side effects and maximizing the speed of emergence. Advances in pharmacology have helped to achieve these goals, but drug delivery methods have evolved very little and are still more art than science. Indeed monitored anesthesia care (MAC) can sometimes resemble “mostly apneic and cyanotic” using current drug delivery methods.¹

The intermittent bolus and constant infusion rates of the present “art” will be replaced by 2050 with more “scientific” methods of drug administration based upon pharmacokinetic and pharmacodynamic principles. Improvements in anesthetic drug pharmacology will certainly continue, but advances in the technology of drug administration will lead the transition from art-based science to science-based art.

Zeroing In on Receptors
Pharmacologic advances in the last several years have focused on improving the pharmacokinetic profile of anesthetic agents. In the future, drug development will enable us to target highly specific receptors. Analgesics will affect specific receptors (peripheral, spinal cord, brain) without stimulating nausea or inhibiting respiration. For instance epibatidine is a novel alkaloid² derived from the skin of the frog, Epipedobates tricolor. Epibatidine analogues are selective agonists at neural nicotinic receptors with analgesic properties totally unrelated to opioid receptors and therefore devoid of respiratory depressant effects. Subpopulations and variations of receptors will be identified by genomics and proteomics during the preoperative visit to enable an individualized selection of drugs and dosages. Furthermore using nanotechnology principles, the present drug solvents will be replaced by physical carriers or in a lyotropic form,³ enabling higher concentrations of drugs to be “loaded” into the “microcages.” This technology enables a longer shelf life as well as confers bacteriostatic properties to the drugs. Even liquid volatile anesthetic agents could be packaged in such microspheres and administered intravenously.

Equipment Makeover
Pharmacologic advances will stimulate changes in anesthesia delivery technology so that the anesthetic equipment in 2050 will be virtually unrecognizable to present-day practitioners. There will be no need for an anesthesia machine for mixing gases and vapors as all anesthetic agents will be administered intravenously with precise control over concentration and effect. Since most “surgeries” will be performed as minimally invasive procedures and respiratory depression will no longer be an unintended side effect, ventilators will rarely if ever be needed. Indeed off-pump coronary artery bypass surgery⁴ and on-pump aortic valve replacement⁵ have already been performed in awake, spontaneously breathing patients.

Instead of the anesthetic vaporizers of today, anesthetics will be delivered using computer-controlled intravenous syringe pumps.⁶ The pumps will be set to obtain a specific target concentration of medication at the effect site, the so-called target-controlled infusion.⁷ In this form of drug delivery, the goal is to maintain a constant concentration (level) of anesthetic drug in a specific pharmacokinetic compartment. To achieve this goal, the infusion pump will be controlled by mathematical models that calculate the infusion rate required to maintain the selected target concentration. The specific target concentration will be selected and adjusted by the anesthesiologist based upon the surgical stimulus. Closed-loop feedback systems⁸ will monitor the actual blood concentrations using noninvasive transcutaneous sensors. A true “depth of anesthesia monitor” will display the activity

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of all nerve pathways conducting the primary stimuli as well as the reticular activating system’s level of arousal. The level of activity in the higher brain centers also will be displayed, and the anesthesiologist will adjust the highly specific drugs to target each nerve pathway and center (spinal cord through brain) to obtain the perfect sedative condition with the assistance of major improvements in digital signal processing given the even more infinitely complex total human physiology of the patient. While digital processing can assist with individual patient complexities, the anesthesiologist will still have to manage the many human interactions in the operating room environments. The higher level of scientific basis of anesthesia in 2050 will therefore require an even higher level of the art of anesthesia than today.

**References:**


**Digital Signal Processing Is Key**

Given the above developments, anesthetic administration will be based on infinitely more complex parameters. Such a multitude of interacting parameters can only be managed for each patient. The art of anesthesia will therefore be based upon scientific measurements. Furthermore all data collected in the operating room will be collated and available to the anesthesia delivery equipment. For instance the blood loss and fluid replacement and their influence on specific vascular beds will be fed to the mathematical models to adjust the pharmacokinetic parameters and improve the accuracy of the calculated body compartment concentrations and rate constants.

Synergism of anesthetic agents will be exploited to ensure maximum drug effect with minimum adverse consequences. At the present time, three-dimensional surface models are available to calculate the interaction between two agents (for instance propofol and fentanyl) and to predict the “time to awakening.” In 2050 multidimensional models will calculate the synergism between many anesthetic agents and suggest appropriate “combinations” of target concentrations: target-guided anesthesia. The art will be to select which set (combination) of targets to use.

This vision of the future of anesthetic delivery mandates that intravenous access be guaranteed for all patients. In 2050 a robotic device will place a peripheral or central line using multiple sensors such as temperature, fluid flow and electromagnetic wave reflections from hemoglobin or other blood constituents to guide the access device. Similar robotic technology will be used through the upper airway to identify and cannulate the tracheas of the few patients who would need an endotracheal tube. The majority of patients will not even require an oxygen-enriched mixture to breathe as respiratory depression will be minimal.

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