CASE STUDY
Chapter 4: Pharmacology of Intravenous Agents

You are asked to provide general anesthesia for an otherwise healthy 30 year-old woman undergoing pelviscopy. She has a history of endometriosis and chronic pelvic pain. Her brother had a near-fatal episode of malignant hyperthermia as a child and she has been counseled to avoid triggering anesthetics. You decide to manage the case with total intravenous anesthesia, avoiding inhalation anesthetics altogether. You have appropriately removed the vaporizers from your anesthesia machine and flushed it with 100% oxygen according to published recommendations.

Which classes of intravenous agents will you need?
As with any anesthetic you need to provide all three components of complete anesthesia: hypnosis, analgesia, and muscle relaxation. No one intravenous anesthetic can provide all three, as can inhalation anesthetics in high enough doses. As you do with balanced anesthesia, you will likely use a combination of drugs which provide primarily one of the three components. You will need a sedative-hypnotic, an opioid analgesic, and a neuromuscular blocking drug.

Which drug will use to produce and maintain unconsciousness? How will you know you’ve given enough? Will the dose needed change during the surgery?
The most commonly used drug in this class for TIVA is propofol, due to its short acting properties and relatively rapid administration after even prolonged administration. Unfortunately, unlike inhalation anesthetics, there is no equivalent of end-tidal concentration to directly monitor effect site concentration. Mathematical models have been developed, however, which closely model this concentration and can be used to control infusion pumps or guide a human operator. In Europe, but not yet in the United States, target controlled infusion pumps exist and can be programmed directly in terms of the desired brain concentration of propofol. When using a manual pump, the dose will indeed be reduced over time in order to maintain such a constant effect site concentration.

Which opioid would be most appropriate for intraoperative use? The case is booked for 2 hours. Will you change to a different agent for postoperative analgesia?
As shown in Figure 4-1, opioids differ markedly in their context-sensitive half times (CSHT; the time required for a 50% decrease in plasma concentration after discontinuing a constant-dose infusion). Therefore, if not using a computerized pump
that holds a constant effect site concentration by decreasing the infusion rate over time, it would be most appropriate to select a drug with a relatively flat CSHT curve. This would include sufentanil, alfentanil, or best remifentanil. The latter, though expensive, is often favored for TIVA because even very high doses (requiring even more than a 50% decrease in concentration) are rapidly eliminated after discontinuation. At the end of the case, you should consider a longer acting drug such as fentanyl, morphine, or hydromorphone to provide postoperative analgesia. The choice may depend on whether the patient will be staying overnight in the hospital (favoring longer acting drugs) or having day surgery (favoring fentanyl).

*Which neuromuscular blocking drug(s) will you choose, if any?*
You will avoid succinylcholine because it is a trigger for malignant hyperthermia. In general, you will intubate and control ventilation in patients undergoing pelviscopy. Therefore, you will use a short-acting and rapid-onset non-depolarizing neuromuscular blocking drug such as vecuronium, rocuronium, or cisatracurium. Given the duration of the case (2 hours), any would be a reasonable choice. For shorter cases, rocuronium is somewhat shorter acting, though more expensive, than the other choices.

*At the end of the case, how will you conduct the emergence?*
This can be the greatest challenge of a TIVA. Because you cannot monitor the concentration of the drugs in the patient’s body, and because there is no well-characterized equivalent of MAC, you must have an understanding of the pharmacokinetics of the drugs in order to allow the patient to awaken promptly at the end of the surgery. You will reverse neuromuscular blockade and discontinue the opioid infusion. If you are using remifentanil, you will consider a small dose of a longer acting drug to provide early postoperative analgesia. Propofol elimination is rapid but not instantaneous; the CSHT is 11 minutes for a one hour infusion plus 4 min per additional hour for propofol, so you will have to carefully monitor the procedure and discontinue it at the appropriate time. Moreover, a 50% decrease in concentration may or may not be sufficient for the patient to awaken, so more or less time may be required. You can monitor the depth of anesthesia with clinical signs (BP and heart rate, signs of sympathetic activation such as tearing or grimace) and with a consciousness monitor such as BIS. You may also decrease the rate of infusion somewhat as surgical stimulation decreases during surgical closure to facilitate emergence once the infusion is halted.