4 / Anesthetic Agents and Anesthesia for Cardiac Surgery

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SEVERAL anesthetic techniques have been advocated for the induction and maintenance of anesthesia for patients undergoing open- and closed-cardiac surgery. In the vast majority of patients, however, anesthesia is induced by use of a rapid-acting barbiturate, followed by the use of a muscle relaxant to facilitate tracheal intubation and produce skeletal muscle relaxation. Analgesia and amnesia are maintained by inhalation or intravenous administration of anesthetics, or both, so that the level of anesthesia suited to the condition of the patient and the needs of the procedure is achieved.

In addition to the usual factors to be considered in the planning of the anesthetic management (for example, previous anesthetic experiences, drug intake, associated pulmonary disease), particular attention should be paid to the status of the ventricular function and the pathophysiologic changes produced by the underlying cardiac disease. With this background knowledge and appropriate monitoring, one can use different anesthetic drugs and adjust the cardiovascular hemodynamics to safely achieve the anesthetic goals.

CARDIOVASCULAR EFFECTS OF ANESTHETIC DRUGS AND NEUROMUSCULAR BLOCKING AGENTS

Some features of drugs are particularly pertinent to the conduct of anesthesia for cardiovascular surgery. A patient's specific disease, previous drug therapy, or previous surgery may alter the dosage of a drug required for a given effect, or even alter the effect itself. Merin[52] addressed himself to this point when he said:

> . . . the only safe way to anesthetize such [patients with diseased hearts] is to adjust the concentration (dose) of whatever anesthetic is used to be comparative with effective ventricular function as determined by the best available monitor(s).

Inhalational Anesthetics

Nitrous Oxide

The dose-effect relationship of nitrous oxide for healthy subjects has been reported: a 20% dose is equivalent to 14 mg of morphine, 40% results in an inability of the patient to cooperate, 60% results in nearly complete amnesia, 80% results in unconsciousness, and 100% results in lack of movement to surgical stimulation (minimum alveolar concentration [MAC][34]). The presence of systemic disease may significantly alter these relationships. The direct effect of nitrous oxide on the myocardium is a depression of contractility.[46] Additionally, nitrous oxide produces signs of increased sympathetic nervous system activity by its action on the suprapontine region of the brain.[29, 54] These signs include peripheral vascular constriction and increased serum levels of norepinephrine.[64] Eisele and Smith[20] substituted 40% nitrous oxide in oxygen for 40% nitrogen in oxygen and showed a decrease of 15% to 20% in cardiac output secondary to decreases in heart rate and contractility. Concomitantly, an increase of 20% in systemic vascular resistance was observed. The net effect on systolic blood pressure was negligible. They also demonstrated elevated levels of circulating catecholamines, especially norepinephrine. Thus, inhalation of 40% nitrous oxide can depress ventricular function in patients without coronary artery disease. In a follow-up study,

Eisele et al.[22] demonstrated that the inhalation of 40% nitrous oxide (after coronary angiography) by patients with coronary artery disease depressed arterial pressure 5% and decreased differential left ventricular pressure (dp/dt) by 14%, with an increase of 21% in left ventricular end-diastolic pressure in patients with impaired left ventricular function.

Nitrous oxide is not a "complete" anesthetic by itself, and, as such, it must be supplemented with other drugs: oxygen, muscle relaxants, and other anesthetics. The weak sympathetic stimulatory and cardiovascular effects of nitrous oxide are still evident when it is combined with other anesthetics in healthy volunteers[34] (Table 4–1); the addition of nitrous oxide to halothane-oxygen anesthesia results in less myocardial depression than that of halothane-oxygen alone.[79] This effect was shown to be in part due to the sympathetic stimulatory effects of nitrous oxide, because the halothane concentration was held constant. An addition of 60% nitrous oxide to 0.55% end-tidal halothane in patients undergoing surgery for aortic and mitral valvular replacements produced no change in mean arterial pressure, right atrial pressure, left atrial pressure, pulmonary artery pressure, heart rate, cardiac index, stroke volume index, systemic vascular resistance, or pulmonary vascular resistance.[79] Stoelting et al.,[79] therefore, recommended 60% nitrous oxide as a useful adjunct to low end-tidal halothane concentrations for valve replacement surgery.

The results are different when nitrous oxide is added to inflow concentrations of enflurane of between 2% and 3%. When the concentration of nitrous oxide reached or exceeded 20%, Bennett et al.[2] demonstrated significant dose-related decreases in cardiac output, stroke volume, and mean arterial pressure. The cardiac depressant effects of nitrous oxide are even more noticeable when it is added to narcotic anesthesia.[92] Stoelting and Gibbs[78] reported that the addition of nitrous oxide to morphine in patients with both valvular disease and ischemic heart disease resulted in a decrease in stroke volume of between 20% and 25%.

Hug[34] noted three actions of nitrous oxide: (1) because it decreases the dosage requirements of other drugs, it limits the cardiovascular effects of these drugs; (2) in the presence of a stable dose of a general anesthetic (particularly halothane), it tends to increase blood pressure by increasing systemic vascular resistance; and (3) the direct cardiac depressant action of nitrous oxide may be masked by cardiac depression induced by volatile anesthetics. This accompanying depressant action may severely limit or preclude the use of nitrous oxide in critically ill patients. If undesirable hypotension occurs during its administration, the inspired concentration of nitrous oxide may be decreased or eliminated completely. Normalization of the blood pressure should be evident within one or two minutes.

Halothane

The potential dose-dependent depression of cardiac function of halothane limits its use as a sole anesthetic agent. In critically ill patients, concentrations of halothane less than 1 MAC can produce anesthesia and potentiate the relaxant effects of nondepolarizing blocking agents.[55] Mechanisms of cardiovascular depression include direct action on cardiac and vascular smooth muscles and depression of the sympathetic nervous system. The primary effect is to inhibit the intensity with which contractile elements generate tension, and a secondary effect is to shorten the duration of the active state of contraction.[5] These effects are accomplished by

TABLE 4–1.—CARDIOVASCULAR CHANGES WITH NITROUS OXIDE AND AFTER ITS ADDITION TO PREEXISTING GENERAL ANESTHETICS

	EFFECT			
MEASUREMENT	NITROUS OXIDE	NITROUS OXIDE–HALOTHANE	NITROUS OXIDE–ENFLURANE	NITROUS OXIDE–MORPHINE
Blood pressure	None	Increased	None	None
Heart rate	Decreased	None	Decreased	Decreased
Cardiac output	Decreased	None	Increased	Decreased
Systemic vascular resistance	Increased	Increased	None	Increased
Central venous pressure	Increased	Increased	None	Increased

an inhibition of the release of membrane-bound calcium involved in excitation-contraction coupling.[5] Halothane has been shown to cause a dose-related depression of isometric (isovolemic) contraction (documented by the use of a strain-gauge arch sewn to the ventricular epicardium[48]) and of isotonic performance (documented by repeat cardiac output determinations[18]). The depression of contractility slowly recovers as the duration of anesthesia progresses,[58] but the amplitude of the I-J wave of the ballistocardiogram does not recover, as does cardiac output.[19] Elevation of the blood pressure during halothane anesthesia does not reverse the depression of ventricular function, thus indicating that cardiac depression is an important part of the mechanism for hypotension.[23] Eger et al.[18] showed a dose-dependent decrease in cardiac output (to 50% of control with 2% halothane) due to equal decreases in stroke volume and contractility. No change was seen in heart rate, but right atrial pressure increased and mean blood pressure decreased along with cardiac output. Theye and Michenfelder[85] determined that total-body and myocardial oxygen consumption decreased along with cardiac output. In patients undergoing coronary artery bypass grafting, halothane for induction decreased the cardiac index by 28%, mean arterial pressure by 22%, and heart rate by 10%.[49]

The depressant effects of halothane may be reversed by intravenously administered calcium, noncatecholamine-containing sympathomimetic agents (ephedrine or mephenteramine), administration of 100% oxygen and hyperventilation to hasten pulmonary excretion, augmented venous return, and anticholinergic agents to treat bradycardia.[34] In certain circumstances, however, the negative inotropic effect of halothane may prove, within limits, to be beneficial. With the fixed coronary blood flow of coronary atherosclerosis, halothane may blunt the increase in myocardial work and oxygen demand that occurs with sympathetic stimulation. Severe decreases in arterial pressure can decrease flow and myocardial oxygen supply. The use of halothane in patients with congestive heart failure is relatively contraindicated.

Cardiac output may additionally be altered by rhythm disturbances, the most common of which are bigeminy, nodal rhythms, and junctional and premature ventricular contractions.[34] Rhythm disturbances are in part due to the effect of halothane in sensitizing the myocardium to circulating catecholamines. Therefore, the dose of exogenous epinephrine should be limited, except for resuscitation purposes, to approximately 1 μg/kg in ten minutes, not to exceed 4 μg/kg/hour.[36]

Although adrenergic blocking agents may increase the sensitivity of the patient to the cardiovascular depressant actions of halothane, treatment with propranolol should be continued up to the time of surgery. The continued presence of propranolol seems to decrease the incidence of severe perioperative dysrhythmias, tachycardia, and hypertension.[41] Continuation of therapy with cardiac glycosides perioperatively is also favored, as it has been demonstrated in dogs that digoxin can antagonize or reverse the cardiovascular depressant effects of halothane.[62]

Enflurane

At equivalent MAC, enflurane produces greater muscular relaxation than does halothane and potentiates nondepolarizing muscle relaxants to a greater degree.[27] Myocardial contractility is decreased in a dose-related fashion, as with halothane; however, the magnitude of depression is greater with enflurane, contrary to early reports. In isolated papillary muscles of the cat exposed to equal MAC of a given anesthetic, Brown and Crout[5] determined the following order of depressant activity, from most to least depressant of contractility:

enflurane > halothane > methoxyflurane > cyclopropane > diethyl ether

In general, heart rate increases and systemic vascular resistance decreases because of decreased activity of the sympathetic nervous system and a direct depressant action on contractile elements, similar to that of halothane. Calverley et al.[6] found that 1 MAC of enflurane decreased cardiac output 26%, stroke volume 40%, systemic vascular resistance 15%, and blood pressure 36%, while heart rate increased 22%. A value of 1.5 MAC of enflurane further decreases stroke volume but not blood pressure or cardiac output. A value of 2 MAC of enflurane could not be achieved without producing profound hypotension. The therapeutic index of enflurane is therefore low, and there is little margin of safety.

The sympathomimetic response seen when

nitrous oxide is added to halothane is not evident when it is added to enflurane.[65] Thus, nitrous oxide offers little protection against the cardiovascular depressant actions of enflurane. As with halothane, the depressant activity may be beneficial in patients with fixed coronary blood flow (presuming coronary perfusion pressure is maintained), because myocardial blood flow decreases in parallel with decreased myocardial work and myocardial oxygen demand.[53]

Sensitization to catecholamines is less with enflurane than with halothane, and dysrhythmias, when they occur, are less severe.[40] In contrast to halothane, enflurane use is associated with cardiovascular instability in patients receiving chronic therapy with propranolol. Horan et al.[33] found greater hemodynamic changes with enflurane when equal anesthetic doses of halothane and enflurane were administered to dogs undergoing propranolol treatment. More impairment of contractility was noted, and loss of blood was tolerated less well; therefore, the concentration of enflurane should be limited in patients receiving propranolol chronically.

In our anesthetic practice, we no longer use other inhalational agents.

Intravenous Anesthetics

Sodium Thiopental (Pentothal)

Thiopental was introduced to anesthetic practice by Lundy in 1934 and has since become the most widely used ultra-short-acting barbiturate for the induction of anesthesia and serves as the prototype of its class. Its cardiovascular effects are dose-related and proportional to the circulating plasma levels. In the patient with a compromised myocardium, the usual large intravenous boluses for induction may produce excessive cardiac depression.

Thiopental is a direct cardiac depressant,[57] and decreased myocardial function is shown by a prolonged preejection period, decreased left ventricular ejection time, and an increased ratio of preejection period to left ventricular ejection time in patients with or without cardiovascular disease.[13] A dose of 4 mg/kg may depress the cardiac index by 10% to 25% and stroke volume by 35%, while heart rate may increase.[47, 86] With thiopental use, the heart rate may increase 19% (36% during intubation), with increases of 30% in cardiac index and of 23% in systolic blood pressure.[86] Venous capacitance may be increased because of decreased sympathetic tone[63] and increased peripheral pooling. The observed decrease in cardiac output may be due to any combination of the following[34]: (1) direct depression of cardiac contractility, (2) decreased filling pressure due to peripheral pooling, and (3) decreased sympathetic outflow from the CNS. The degree of hypotension is reduced by compensatory increases in heart rate and peripheral vascular resistance (32%).[8] The speed of injection influences the degree of hypotension. With slow infusions, there is time for compensatory mechanisms to become effective. Decreases in arterial pressure are seen within 90 seconds, and recovery begins by three minutes.[26] The desired depth of anesthesia can be reached with incremental doses of 0.5 to 1 mg/kg, and the magnitude of cardiac changes is minimized.

In patients with poor left ventricular function, thiopental may induce further impairment of contractility. The drug selected for induction should produce little or no cardiac depression (for example, fentanyl or diazepam). The existence of fixed coronary flow with good left ventricular function may be an indication for thiopental, as myocardial oxygen consumption will be decreased by the negative inotropic effects, if it is assumed that the compensatory tachycardia is blocked (for example, by propranolol).

Diazepam

Induction as well as anesthesia may be accomplished with diazepam. Although most patients may tolerate as much as 1 mg of diazepam per kilogram of body weight, some patients experience depression of respiratory and cardiovascular function when much lower doses are used.[34] Low doses of diazepam (0.13 mg/kg) have little effect on cardiac output, while large doses (0.77 mg/kg) decrease stroke volume by 30%.[80] A decrease in cardiac output secondary to the decrease in stroke volume is noted, and this is associated with a decrease of between 5% and 20% in arterial pressure.[34]

The cardiac depressant effects of diazepam are more evident when the drug is used with a narcotic. A dose of 5 mg of diazepam after morphine administration (2 mg/kg) produced decreases in heart rate and mean arterial pressure, with an increase in peripheral vascular resistance.[70] A second dose of diazepam further re-

duced systolic blood pressure. After 50 μg of fentanyl per kilogram, 10 mg of diazepam decreased stroke volume, cardiac output, blood pressure, and peripheral vascular resistance and increased central venous pressure with no change in heart rate.[68] Thus, cardiovascular depression can be seen when diazepam is given after morphine and fentanyl.

Increases in coronary blood flow have been noted after the administration of diazepam, and the increase was greater in patients with coronary artery disease than in normal subjects.[35] Diazepam also decreases left ventricular end-diastolic pressure by as much as one third in patients whose values were increased previously.[11] Decreases in myocardial oxygen consumption and left ventricular stroke work also have been found after the administration of diazepam. Small incremental doses (2.5 to 5 mg) intravenously, titrated to effect, are advocated for induction.

Droperidol

The concept of neuroleptanalgesia was introduced by de Castro and Mundeleer[14] in 1959. In 1966, Foldes et al.[28] used the term "neuroleptanesthesia" to describe the addition of nitrous oxide to droperidol and fentanyl, and it is in this context that droperidol is often used. Droperidol (dehydrobenzperidol) is a butyrophenone, and, like other major tranquilizers, can produce a neuroleptic state that is characterized by suppression of affect, slowing of motor function, and an outwardly calm appearance. The half-life of droperidol is 2 to 3 hours, and its duration of effect is 6 to 12 hours; the usual pharmacologic agents do not reverse its effect. In addition to its tranquilizing properties, droperidol has an antiemetic effect, reduces total-body oxygen consumption by 25% with a 10-mg dose, and suppresses temperature-regulating mechanisms.[34] Because its effect on sedation is variable, droperidol should be used with other drugs to provide anesthesia.

After the administration of droperidol, hypotension may occur on the basis of depression of the central nervous system and α-adrenergic blockade. The intravenous injection of 0.15 mg of droperidol per kilogram produces a transient decrease in arterial pressure.[89] Direct aortic injection produces an immediate decrease in blood pressure because of α-adrenergic blockade. Muldoon et al.[56] showed that concentrations of droperidol that are α-adrenergic blocking do not depress myogenic contractility. Injection of 2.5 mg of droperidol after 2 mg of morphine per kilogram increased heart rate and cardiac output, with a decrease in peripheral vascular resistance.[70] These changes were not present after five minutes. In one study, a dose of 5 mg of droperidol injected into patients receiving an enflurane-nitrous oxide-oxygen anesthetic decreased systemic vascular resistance and blood pressure and increased heart rate and total blood flow.[66] The changes were maximal in five minutes and returned to control in 15 minutes. Thus, small amounts of droperidol produce significant, although transient, decreases in blood pressure and systemic vascular resistance, similar to the changes seen with halothane and morphine.

Injection of droperidol into the oxygenator during cardiopulmonary bypass decreases blood pressure, and when the droperidol effect is maximal, the pressor response to epinephrine and norepinephrine is suppressed.[69] This effect suggests that droperidol may be a generalized adrenergic blocking agent, in addition to its α-adrenergic blockade. Droperidol also has an antiarrhythmic effect. Long et al.[43] found that 0.2 mg/kg doubled the arrhythmic threshold for epinephrine-induced dysrhythmias. Low doses of droperidol (250 μg/kg) prevented epinephrine-halothane–induced arrhythmias in cats without inhibiting the increase in blood pressure—an activity independent of α-adrenergic blockade.[3] Induction of ventricular fibrillation by coronary occlusion also was prevented. Similar to quinidine, droperidol lengthens the effective refractory period.[3] This effect is not reduced by doses of norepinephrine sufficient to induce positive inotropic effects.

The effects of droperidol in cardiac patients were summarized by Ferrari et al.,[25] who found that 0.25 to 0.5 mg/kg decreased systemic vascular resistance, central venous pressure, and arterial pressure without negative inotropic effects. Thus, droperidol may be useful in the digitalized patient with congestive heart failure or in the patient with congestive heart failure who is likely to develop arrhythmia.

Narcotic Agents

Narcotics are not anesthetics, and although anesthesia and apnea may be induced, unconsciousness may not be rendered. Supplementa-

tion of these drugs with depressants of the CNS and muscular relaxants is common and reduces the risk of intraoperative awareness, decreases skeletal muscle rigidity, provides surgical relaxation, and decreases the required dose of the narcotic.

MORPHINE.—In 1965, Lowenstein[44] introduced the practice of intravenously administering large doses of morphine (0.5 to 3 mg/kg) for cardiac surgery. Subsequent studies showed that 1 mg/kg intravenously did not affect cardiac output, systemic vascular resistance, blood pressure, central venous pressure, or heart rate in healthy patients but decreased systemic vascular resistance and increased cardiac output in patients with aortic valve disease.[52]

Hypotension may occur after the administration of morphine and may be secondary to bradycardia, release of histamine, or depression of the sympathetic nervous system.[34] Bradycardia may be secondary to increased vagal activity and is corrected by the use of an anticholinergic agent. Release of histamine is variable in incidence and severity, and its consequences are minimized by the slow injection of morphine and by circulatory support. Assisted ventilation during induction to prevent the accumulation of carbon dioxide is desirable. Hypotension secondary to sympathetic depression may be overcome by vasopressors or intravenously administered fluids (or both). The use of morphine increases the intraoperative requirements for intravenous fluids and transfusions.[60]

Morphine neither directly depresses myocardial and vascular smooth muscle nor sensitizes the heart to catecholamines nor predisposes to arrhythmias.[34] The net hemodynamic effect is dependent on the circulating blood volume—if the volume is below a certain threshold value, the decreased resistance and increased capacitance may stimulate baroreceptors and produce a catecholamine-induced vasoconstriction, with a secondary decrease in cardiac output.[45] The myocardial depressant and sympathomimetic effects of nitrous oxide are evident when it is added to morphine. Martin et al.[50] observed decreased cardiac output and increased systemic vascular resistance when nitrous oxide was added to morphine. In patients with coronary artery disease, the addition of 60% nitrous oxide decreased blood pressure by 25% and cardiac output by 17%.[78] Prior administration of barbiturates may invalidate the assumption of relatively benign cardiac effects of morphine. Stoelting[75] found that, after induction with 4 mg of thiamylal per kilogram, the administration of 1 mg of morphine per kilogram resulted in a decrease of 16% in mean arterial pressure, a decrease of 42% in cardiac index, and an increase of 35% in systemic vascular resistance. Morphine, when used judiciously and combined with drugs that minimally depress the heart, is an excellent anesthetic for cardiac surgery.

MEPERIDINE.—Meperidine is approximately one tenth as potent as morphine and has a shorter duration of action. Hypotension may occur owing to a negative inotropic effect, decreased systemic vascular resistance, and decreased venous return secondary to increased capacitance or bradycardia.[34] Meperidine has a direct depressant effect on contractility that is approximately 200 times greater than that of morphine.[82] In anesthetized patients, bradycardia and decreases in systolic blood pressure may be observed.[24] Meperidine in a dose of 2 mg/kg in dogs decreased cardiac output by 30%, secondary to decreases in stroke volume and heart rate; however, systemic vascular resistance and pulmonary vascular resistance were significantly increased.[31] The initial dose is 1 to 3 mg/kg, supplemented with approximately 0.5 mg/kg as needed.

FENTANYL.—Fentanyl is approximately 100 times more potent than morphine and 1,000 times more potent than meperidine, and has a shorter duration of action, at least after a single dose. Its onset of action is almost immediate, and the effects of a single dose are dissipated within 30 minutes.[51] Compared with the effect with morphine administration, histamine release is negligible, and there is less increase in venous capacitance. The primary cardiac effect is bradycardia, which is prevented by the use of atropine[21] and minimized by slow infusion, especially during induction.[68] Equal analgesic doses of morphine and fentanyl decrease heart rate similarly, but the decrease in blood pressure is much less with fentanyl.[51] No negative inotropic effect is evident, and sympathetic responses with associated tachycardia and hypertension are suppressed.[34]

Fentanyl in doses of 20 μg/kg decreased heart rate and blood pressure but did not change

stroke volume, cardiac output, central venous pressure, or peripheral resistance.[68] No further changes were seen when the dosage was increased from 20 to 50 μg/kg. At a dose of 10 μg/kg, no significant circulatory changes were seen. Unresponsiveness was observed at a dose of approximately 11 μg/kg. The total dose for mitral valve replacement averaged 74 μg/kg.[68]

Tarhan et al.,[84] using droperidol and fentanyl in a ratio of 50:1 for analgesia and sedation during coronary angiography, observed a decrease of 11% in systemic vascular resistance, a decrease of 9% in mean arterial pressure, a decrease of 11% in total-body oxygen consumption, and no change in cardiac index. Stoelting et al.,[80] using fentanyl (10 μg/kg) or fentanyl (10 μg/kg) and droperidol (100 μg/kg), found minimal changes in circulatory dynamics in adults with acquired valvular disease. An increase in central venous pressure was noted during infusion of the drug; the pressure decreased to awake levels after controlled ventilation and skeletal muscle relaxation. They believed that this reflected thoracoabdominal muscular rigidity rather than a circulatory response. The addition of 60% nitrous oxide after either of the above regimens significantly decreased mean arterial pressure, heart rate, and cardiac index.

Fentanyl has a large therapeutic index, and its major cardiovascular effect (bradycardia) is easily corrected. Vascular tone is preserved better than with morphine. Cardiovascular depressant effects of adjuvant drugs (for example, nitrous oxide) are rarely seen. Thus, fentanyl is an entirely reasonable choice for cardiac anesthesia.

Ketamine

Ketamine is a cardiovascular stimulant and increases blood pressure, heart rate, and cardiac output. Its stimulatory effects follow the course of its anesthetic effects. Coppel and Dundee[10] showed that the stimulatory response to ketamine had dissipated by 16 minutes after injection and that subsequent injections did not produce a further increase in pressure. The mechanism of stimulation is complex and includes increased sympathetic outflow and impairment of baroreceptor reflexes. Tweed et al.[87] showed that a dose of 2 mg/kg produces an increase of 30% in mean arterial pressure, heart rate, and cardiac index, thus enhancing myocardial contractility. This increase is associated with increased cardiac work and an increase in myocardial oxygen consumption. Therefore, ketamine should not be used in patients with coronary artery disease and should be administered with caution to patients with severe myocardial disease of any type. Increases in pulmonary artery pressure and pulmonary blood flow also are seen with ketamine, but these increases are related to the increased cardiac output rather than to a change in the pulmonary vasculature.[30]

Because it increases cardiac output without a large decrease in systemic vascular resistance, ketamine may be a desirable agent in patients with hypovolemia, hemorrhage, or shock (as in traumatic injury to the heart or great vessels). When an increase in mean arterial pressure is undesirable, the use of ketamine is contraindicated. Ketamine also may be of value as an induction agent for patients with constrictive pericarditis.[38] These patients have a low cardiac output and increased central venous pressure due to the pericardial restriction. The minimal depressant actions of diazepam are accentuated in these patients, while ketamine may help maintain circulatory dynamics.[38] The induction of a pediatric cardiac patient who has a right-to-left shunt may proceed more rapidly with ketamine than with inhalational agents.[59] Ketamine is seldom used in our clinical practice.

Neuromuscular Blocking Agents

Succinylcholine

Small and inconsistent hemodynamic effects are seen after the administration of succinylcholine.[32] Bradycardia may occur and is more common with halothane anesthesia.[90] The presence of hyperkalemia or conditions that may result in hyperkalemia with succinylcholine administration (burns, tetanus, upper motor neuron disease, and so forth) predisposes to the development of arrhythmias.

d-Tubocurarine

Intravenously administered *d*-tubocurarine produces a dose-related hypotension due to a decrease in systemic vascular resistance. The decrease in systemic vascular resistance is based on the release of histamine. Another action of *d*-tubocurarine is blockade of the sympathetic ganglia.[17] Halothane and hypovolemia enhance the

hypotensive effects of *d*-tubocurarine,[7, 73] which are readily corrected by the administration of fluids or vasoconstrictors.

Pancuronium

Pancuronium is the most potent clinically available neuromuscular blocker. Its cardiac actions include an increase in heart rate and, therefore, result in secondary increases in cardiac output and systolic blood pressure, while systemic vascular resistance remains unchanged. When boluses of pancuronium are given rapidly, tachyarrhythmias tend to develop. This effect is not a problem with the slow intravenous administration. Histamine release is not seen with pancuronium.[15] When pancuronium is added to enflurane anesthesia, a decrease of 10% in cardiac index and a decrease of 20% in stroke volume can be demonstrated.[39] This result contrasts with the effect of administering pancuronium during halothane, in which an increase in cardiac index is seen with an increase in heart rate.[71]

Gallamine

Gallamine produces tachycardia by vagal blockade and releases norepinephrine limited to the cardiac sympathetic nerves.[4] Associated with the tachycardia is an increase in cardiac output and systolic blood pressure, with a decrease in systemic vascular resistance.[72] Because of this effect, the use of gallamine is limited to treatment before intubation using succinylcholine.

Metocurine

Metocurine promises to be the most useful neuromuscular blocker for cardiac anesthesia. It was first synthesized by King[37] in 1934 as a trimethylated derivative of *d*-tubocurarine, and its chemical name is dimethyl tubocurarine. Metocurine was introduced into clinical practice in 1948 by Stoelting, Graf, and Vieira[81] and Wilson, Gordon, and Raffan.[91]

Metocurine has an ED_{50} and an ED_{95} for twitch inhibition of 0.13 and 0.28 mg/kg, respectively.[61] The potency ratio of metocurine is 0.25 compared with pancuronium and 1.8 compared with *d*-tubocurarine (Table 4–2). Recovery to 25% of control twitch height takes approximately 82 minutes.[61] No changes in heart rate or mean arterial pressure are seen until the dose reaches 0.4 mg/kg; then the rate increases by 18% and the mean arterial pressure decreases by 6%, suggestive of histamine release (which was shown in 6 of 18 patients[61]). Cardiac muscarinic receptors are not blocked.

TABLE 4–2.—COMPARATIVE POTENCIES AND TIMES TO RECOVERY OF 25% OF ORIGINAL TWITCH HEIGHT*

AGENT	ED_{95}, MG/KG	RECOVERY OF 25% TWITCH HEIGHT	
		DOSE, MG/KG	TIME, MIN
Metocurine	0.28	0.3	82.4
d-Tubocurarine	0.51	0.6	80.5
Pancuronium	0.07	0.1	99.3

*Data from Savarese et al.[61]

During deep levels of enflurane–nitrous oxide–oxygen anesthesia, modest doses sufficient to abolish thumb adduction have little influence on cardiovascular dynamics.[67] Anesthetic technique alters the dose required: Savarese et al.[61] reported 0.28 mg/kg as the ED_{95} for morphine–thiopental–nitrous oxide, Stoelting[73] reported 0.2 mg/kg as the ED_{95} for halothane–nitrous oxide–oxygen, and Stanley[67] reported 0.12 mg/kg as the ED_{95} for deep enflurane–nitrous oxide–oxygen anesthesia. Enflurane anesthesia seems to potentiate the action of metocurine. In the presence of propranolol treatment, 0.35 mg of metocurine per kilogram produced a decrease of 20% in systemic vascular resistance. This effect resulted in an increase of 26% in cardiac output, with a corresponding increase in stroke volume to maintain coronary perfusion pressure. No change was seen in mean arterial pressure, heart rate, or central venous pressure.[93] Because of the minimal effects on cardiovascular dynamics, metocurine may be the relaxant of choice for cardiac anesthesia.

INDUCTION OF ANESTHESIA

Induction of the Adult Patient

Patients with cardiac disease tolerate much less depression of their circulation than do normal, healthy subjects. Fortunately, the depth of anesthesia required by most cardiac patients undergoing open-heart surgery is also much less than that needed for a patient without cardiac disease.[83] Occasionally, patients undergoing car-

diac surgery are critically ill, and a successful outcome for such patients demands scrupulous attention to every detail of their perioperative management. This approach has been helpful in the development of anesthetic techniques that are suited to all critically ill patients undergoing noncardiac operations and fulfilling the classic triad of anesthetic goals: analgesia, amnesia, and skeletal muscle relaxation. Induction of anesthesia in the operating room is greatly facilitated by appropriate preoperative medication (see chap. 3).

In the management of the adult patient undergoing elective cardiac surgery, monitoring of the vital signs should begin as soon as the patient arrives in the operating room. A blood pressure cuff is applied to either one of the upper extremities, and the initial pressures are obtained. If the patient has had previous bilateral Blalock-Taussig shunts, the blood pressure cuff should be applied to one of the lower extremities. Electrocardiographic leads are attached, and the ECG is displayed continuously on an oscilloscope throughout the procedure. The V_5 lead is monitored to provide early indication of ventricular ischemia. In each upper extremity, intravenous routes are established with large-bore 14- or 16-gauge Teflon catheters. After testing for the adequacy of collateral circulation by means of a modified Allen test, an 18- or 20-gauge Teflon catheter is inserted percutaneously into the radial artery under local anesthesia. Generally, the use of the artery on the side of a previous brachial arteriotomy for cardiac angiography is avoided. The femoral arter, can alternatively be cannulated percutaneously with a 10- or 15-cm Teflon catheter or with a long catheter advanced into the thoracic aorta by means of the Seldinger technique.[88] Catheterization of the femoral artery is usually done with the patient anesthetized, but can be done under local anesthetic infiltration if necessary. After intubation in patients without compromised left ventricular function and before intubation in patients with left ventricular dysfunction, a central line is established using either the internal jugular vein or external jugular vein, with a modified Seldinger and J-wire technique. A Swan-Ganz catheter, if necessary, is also inserted at this time. If a Swan-Ganz catheter is used, a Cordis introducer sheath is used because the side port allows an additional infusion site.

With these preliminary steps accomplished, the induction of anesthesia can begin. Small incremental doses of thiopental (50 to 75 mg), as needed and as tolerated, are given slowly until the lid reflex is obtunded. Critically ill patients usually require small doses of thiopental to achieve hypnosis, thus decreasing the chances of significant myocardial depression so well known to all anesthesiologists.[16]

Next, the trachea is intubated with a low-pressure cuff endotracheal tube. In our current practice, this is preceded by an intravenous injection of pancuronium (0.08 to 0.1 mg/kg) during the induction with thiopental, and three to five minutes are allowed to elapse before intubation is attempted. Succinylcholine (1.5 mg/kg) or metocurine (0.35 mg/kg) may be used intravenously, depending on the clinical situation. Before endotracheal intubation, 2 to 4 ml of 4% lidocaine is applied topically to the trachea to attenuate the circulatory changes produced by direct laryngoscopy and tracheal intubation.[74, 76] Less frequently, sodium nitroprusside, administered either in a single rapid intravenous injection (1 to 2 μg/kg) or in an intravenous drip, has been used to achieve the same purpose.[77]

After intubation, the patient is mechanically ventilated to keep the $PaCO_2$ between 35 and 40 mm Hg. There are different techniques for the maintenance of anesthesia. Generally, to achieve the anesthetic goals for cardiac surgery in a given patient, we use nitrous oxide–oxygen (50:50) supplemented with a volatile anesthetic (halothane or enflurane), an intravenous narcotic (meperidine, morphine, or fentanyl), or an intravenous tranquilizer (droperidol or diazepam).

The choice of anesthetic agent for a specific patient should reflect the patient's status, the disease, and the known drug effects. Either inhalation agent, halothane or enflurane, may be used in patients with fixed coronary flows or in patients in whom a mild decrease in contractility would not be disastrous. Narcotic techniques are more appropriate for patients with limited cardiac reserve. In these patients, fentanyl may offer advantages over morphine, because the risk of histamine release is much less and a negative inotropic effect is not evident.[34] Usual induction techniques should be altered before the use of a narcotic, because barbiturate induction followed by morphine administration may result in significant decreases in mean arterial pressure, cardiac index, and stroke volume index while increasing systemic vascular resistance.[75]

The choice of narcotic supplement should be carefully considered, because the addition of nitrous oxide to morphine may produce significant cardiovascular depression.[78] Scopolamine, 0.5 mg intravenously, may increase heart rate, stroke volume, cardiac output, and blood pressure during morphine-nitrous oxide anesthesia.[1] At the same time, central venous pressure and peripheral vascular resistance may decrease. Scopolamine may be a more effective supplement than nitrous oxide during high-dose morphine anesthesia; however, diazepam or droperidol also can be used safely as a supplement.[70]

The choice of muscle relaxant should receive equal consideration. While the use of succinylcholine in the acutely hypotensive patient allows reflex sympathetic stimulation and an increase in blood pressure, these effects are totally undesirable in the patient with fixed coronary flows or minimal cardiac reserve. Pancuronium may be useful in the patient in whom bradycardia is a problem; however, the increase in rate may severely increase myocardial oxygen consumption. The hypertensive patient could benefit from the histamine release associated with *d*-tubocurarine, but a stroke or heart failure may occur in the patient with borderline compensation. For patients unable to tolerate a change in their hemodynamic state, metocurine may be the agent of choice.

There is no universal anesthetic or relaxant, and thus no panacea for cardiac anesthesia. The selection of agents for a specific patient involves clinical judgment and acumen, as well as a detailed knowledge of the hemodynamic effects of the particular drugs. When these factors are considered, one can follow the dictum of *primum non nocere* and make active interventions to improve the patient's status.

Induction of the High-Risk Cardiac Patient

"High-risk" patients usually are so critically ill that most of them will not tolerate the usual stress of anesthetic induction and may not be able to maintain their hemodynamic homeostasis until cardiopulmonary bypass is instituted. These patients usually have a combination of intractable heart failure and advanced pulmonary, renal, or hepatic disease.[12]

Once the patient arrives in the operating room, the usual monitoring is started. Under local anesthesia, intravenous, intra-arterial, and central venous lines are established. Small increments of sedative drugs (diazepam) or narcotics (morphine, meperidine, or fentanyl) are given concurrently. After the skin is prepared, the patient is draped, the instrument tables are brought into position, and the appropriate lines are connected to the cardiopulmonary bypass machine. Under local anesthesia, the right femoral vessels are exposed. The patient is fully heparinized, and a long venous cannula and the usual short arterial cannula are inserted. If needed, the opposite femoral vein may be cannulated and connected to the venous line to improve venous drainage. After these preparations, cardiopulmonary bypass may be instituted at any time, depending on the condition of the patient.

In these critically ill patients with precarious hemodynamics, cardiopulmonary bypass should be instituted and anesthesia simultaneously induced with thiopental (300 to 500 mg) or diazepam (20 to 40 mg) followed by succinylcholine (100 to 150 mg) and tracheal intubation without undue rush, because the cardiopulmonary functions already have been bypassed. The required amnesia-analgesia and adequate skeletal muscle relaxation then can be established. Although most cardiac patients require relatively light planes of anesthesia, this special group of high-risk patients requires mainly adequate paralysis with amnesia-analgesia and great efforts at resuscitation. In recent years, we have used intra-aortic balloon support before the induction of anesthesia in selected patients to maintain myocardial blood flow and to decrease afterload of a compromised ventricle.[9, 42] These measures should reduce the operative mortality and perioperative myocardial infarction rate.

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