Rationale: All of the trials evaluating the most appropriate size descriptor for dosing NMBAs in severely obese patients were single-dose studies conducted in the perioperative setting (185–194). The primary endpoint for these studies was either pharmacokinetic or pharmacodynamic (e.g., muscle recovery based on TOF monitoring) in nature. Therefore, no information is available regarding whether the choice of a size descriptor may influence outcomes or length of stay parameters when NMBAs are used on a sustained basis in the ICU setting. Despite these caveats, the results of the studies do provide guidance for weight-based dosing regimens of NMBAs. In a double-blind randomized study (185) involving 20 severely obese patients (body mass index 38–79 kg/m^2) undergoing bariatric surgery, atracurium dosing based on ideal body weight resulted in significantly shorter recovery time by TOF monitoring and less variability in recovery, compared with dosing based on actual body weight. There was a dose-dependent prolongation of recovery time using actual body weight that was not seen with ideal body weight; furthermore, none of the patients in the ideal body weight group required neostigmine at the end of the operation, compared with 70% of patients who were dosed using actual body weight. These results are consistent with findings from other open-label trials involving atracurium, cisatracurium, vecuronium, and rocuronium, all of which suggest that dosing should not be based on actual body weight (189, 190, 192–194). In contrast, small open-label trials that evaluated NMBA dosing in obese versus nonobese patients did not find differences in recovery times (186, 187, 191). However, one of these trials found nonproportional increases in the volume of distribution of atracurium and total clearance with increasing weight, suggesting actual body weight should not be used for dosing (187). In the other trials (186, 191), severely obese patients were not included, making it difficult to detect differences based on weight-based dosing. A final, small (n = 14), open-label trial of pancuronium in morbidly obese and normal-weight patients (188) did not evaluate recovery time and had analysis concerns (195).

The authors of these trials recommended against the use of actual body weight and uniformly recommended using ideal body weight for weight-based dosing of NMBAs. Ideal body weight has the advantage that it is easy to calculate. However, ideal body weight is a surrogate for lean body weight. Lean body weight has been evaluated prospectively for drug-dose prediction in obese patients, but its use requires more complex equations that are far less commonly used in the clinical setting (196). Given other problems related to weight estimates and changes over time in the ICU setting, the continued use of ideal body weight seems reasonable until equations based on lean body weight have been evaluated in critically ill obese patients. An adjusted weight that takes into account a portion of the excess weight might be a reasonable alternative. Importantly, clinicians should strive for consistency in weight measurement and choice of weight among patients and for a single patient when using weight-based dosing for NMBAs (197, 198).

Pregnant Patients. XIX. Can continuous NMBA infusions be used in intubated and mechanically ventilated patients who are pregnant and have an indication for the administration of an NMBA?

Response: We make no recommendation on the use of NMBAs in pregnant patients (insufficient evidence).

Rationale: NMBAs have been used extensively in pregnant patients for obstetrical and nonobstetrical surgeries. Cisatracurium and rocuronium are the only NMBAs that are listed as pregnancy category B drugs. Their use is based on a clinical decision that an NMBA may be justified to save the mother's life or to avoid severe hypoxia for both the mother and the fetus. In the ICU where longer-term use may be encountered, the use of category C drugs should be avoided because category B drugs are available. All NMBAs or their metabolites, with the exception of cisatracurium, cross the placental barrier.

There are no double-blind, randomized, controlled trials comparing NMBAs in pregnant critically ill patients. Most studies of NMBAs administered to pregnant patients have been conducted in patients undergoing cesarean sections or other surgery that requires only one or two doses of an NMBA. An older report associated long-term fetal exposure to NMBAs with arthrogryposis (199). NMBAs are sometimes necessary in the critically ill pregnant patient with ARDS. Critically ill obstetrical patients have increased risk of death from respiratory failure, with an OR of 12.9 for mortality (200), and have a fetal loss rate of 34–52% (200, 201). ARDS alone is associated with a 12% rate of fetal loss (201). Delay in ICU care was found to have an OR of 2.3 for maternal mortality in obstetrical patients (202). Maternal clinical indicators should guide treatment decisions as in these patients. There has been an association between first trimester surgery and low fetal birth weights and increased fetal loss, but no association with any actual drug has been identified (203–205).

The decision to use NMBAs cannot be made purely on whether NMBAs cross the placenta because NMBAs are found in varying concentrations in fetal blood and thus do cross the placenta (206). Historically, succinylcholine was the NMBA of choice for obstetrical procedures because even though it crossed the placenta it had minimal if any clinical effects on the neonate (207). Vecuronium has been shown to have residual clinical effects in the newborn (208), and atracurium and rocuronium also have placental transfer (209, 210). Similar to succinylcholine, pancuronium, atracurium, and vecuronium all cross the placenta and are pregnancy class C, their use should be avoided for long-term infusion, especially in the first trimester (208, 211–214).

Vecuronium, atracurium, and rocuronium do not have a prolonged clinical effect in the pregnant or postpartum patient (208, 210, 215). Cisatracurium has been shown to have a shorter duration of effect in the immediate postpartum patient than in the nonpregnant patient (216). When metabolized, atracurium and cisatracurium produce plasma concentrations of laudanosine, a neuroactive metabolite with the potential to precipitate seizures, but atracurium is associated with much higher levels of laudanosine than cisatracurium (217).

Brain Death. XX. Can clinicians determine brain death in patients receiving NMBAs?