

# Discrepancies in IV Epinephrine Use: A Newsmaker Interview With Lisa M. Sullivan, MD

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Nov. 10, 2003 — *Editor's Note: Discrepancies, confusion, and error surrounding intravenous (IV) epinephrine use increase the risk of over- or underdosing, according to a presentation on Nov. 10 at the American College of Allergy, Asthma and Immunology annual meeting held in New Orleans, Louisiana.*

*Although investigators have long suggested that all drugs, especially those used in emergencies, should be measured in a standard way to avoid dosing errors, epinephrine and most other resuscitation drugs are not. A review of the medical literature and the databases of Rush University and Northwestern University in Chicago revealed numerous inconsistencies for the recommended dosage of intravenous epinephrine, typographical errors resulting in published dosages 10 to 100 times more or less than intended, confusing terminology for dosages, case reports of epinephrine overdose, and errors in physician calculations.*

*To improve patient safety, coauthors Lisa M. Sullivan, MD, and Anita Gewurz, MD, recommend using the microgram as the mass unit for quantitating epinephrine, standardizing dosing guidelines for IV epinephrine, and spelling out "microgram" or avoiding use of the Greek "mu."*

*To learn more about the implications of this study, Medscape's Laurie Barclay interviewed Dr. Sullivan, a fellow in allergy, asthma and immunology and an instructor in pediatrics at Northwestern Feinberg School of Medicine and Children's Memorial Hospital in Chicago, Illinois. The authors have no financial disclosures, and the Rush University and Cook County combined training program in allergy, asthma and immunology helped sponsor Dr. Sullivan's participation in the study.*

Medscape: What were the main findings of this study?

**Dr. Sullivan:** Numerous problems surround IV epinephrine dosing. The first is antiquated labeling. Many drugs used for resuscitation date back to before the 1938 Food, Drug and Cosmetic Act, and thus are not subject to current Food and Drug Administration (FDA) labeling standards. Epinephrine is marketed and dosed as a dilution ratio, mass concentration, volume concentration, or percentage concentration. These conventions are antiquated and prone to error, with case reports of accidental overdose all too common. Physicians, anesthesiologists, residents, and nurses have administered the wrong dilution because 1:1,000 and 1:10,000 look similar and often occupy the same tray. Labels also lack warnings to dilute the 1:1,000 concentration before IV administration.

The second source of error is physician prescribing. A number of studies describe frequent problems with physician calculations, dilution conversions, and decimal use. By current convention, these are all required for IV epinephrine dosing.

The third finding is typographical errors in publications. We found many typographical errors that resulted in IV epinephrine doses that were off by a factor of 10 to 1,000. These were in all types of publications, from practice parameters of well-known groups to journal articles to both [print] and online textbook chapters dedicated to the treatment of anaphylaxis.

Finally, we were able to locate vast inconsistencies for the recommended dose of IV epinephrine for anaphylaxis and other life-threatening emergencies. Literature with the correct dosing was often confusing, expressing the dose in either a volume or a mass with varying dilutions. Concentrations of solutions were rarely given. Frequently, units were switched mid-paragraph without reference to unit conversions. Administration details such as rate and maximum dose were omitted.

These opportunities for calculation error, typos, ambiguity in IV epinephrine dosing, and dilution labeling represent significant risks for overdose, or underdose, in an already life-threatening situation.

Medscape: What are the risks of variable dosing of IV epinephrine?

**Dr. Sullivan:** IV epinephrine is the drug of choice when anaphylaxis is profound and life-threatening and vascular access is available. For anaphylaxis, a low dose, slow infusion rate has life-saving effects. These include bronchodilatation, chronotropic cardiac activity and positive inotropic effects (beta effects), while increasing peripheral vascular resistance, reversing peripheral vasodilation, reversing systemic hypotension, and reversing vascular permeability (alpha effects). A high dose, high infusion rate has adverse effects. Alpha-agonist effects predominate resulting in excessive vasoconstriction. This compromises extremity, mesenteric, and renal blood flow and results in severe [hypertension](#), leading to intracerebral hemorrhages, myocardial infarctions, and possibly death.

Therefore, too low of a dose would compromise the resuscitation effort, allowing [anaphylactic shock](#) to run its course, increasing the morbidity and mortality of the event. Too high of a dose would also increase the morbidity and mortality by iatrogenic means.

Medscape: How can patient safety be improved?

**Dr. Sullivan:** First, standardize labeling of epinephrine. Vials should clearly state micrograms/mL, regardless of dilution. For example, 1:1000 equals 1,000 mcg/mL, 1:10,000 equals 100 mcg/mL, and 1:100,000 equals 10 mcg/mL.

Second, use the microgram as the mass unit for comparison. All doses quoted in the literature currently fall between 0.1 to 5,000 micrograms, with the majority of dosing in the 1 to 500 mcg range. This would eliminate most decimal calculations, extra zeros, and unit conversions.

Third, universalize IV epinephrine dosing guidelines. Indicate the IV dose as a rate; use micrograms/minute for adults and micrograms/kg/minute for children; outline the timeframe for administration; and state the maximum dose.

Fourth, review all articles on IV epinephrine recommendations with caution. Pay close attention to dose units, dilutions, and watch for typos. Published doses may be off by a factor of 10 to 1,000.

Fifth, spell out microgram or abbreviate "mcg" for both handwritten and typed doses. The Greek symbol mu can inadvertently be changed to an "m" during any part of the publication process. A handwritten Greek mu may also be mistaken for an "m."

Medscape: How can these recommended changes best be implemented?

**Dr. Sullivan:** On a national scale, one would first request that the FDA mandate better labeling for all epinephrine products, that is, mcg/mL. Practice parameters would then need to be in place to include these recommendations. Physicians would then need to be made aware of these changes. The changes would also need to be incorporated into training programs and continuing education classes. On a small scale, individual hospitals, offices, and their pharmacies may wish to label their own epinephrine and train hospital employees to use this easier and safer method of IV epinephrine dosing.

Medscape: Do you anticipate widespread acceptance of recommended changes and implementation of the changes into routine practice?

**Dr. Sullivan:** Based on the response that I have received thus far, I do anticipate widespread acceptance of these recommendations. However, unless regulatory agencies get involved, I would guess that it would be difficult to change such an antiquated system.

Medscape: Are there lessons to be learned from this study with regard to the dosing conventions of other drugs?

**Dr. Sullivan:** Absolutely. The same problems surely exist for many of the older resuscitation drugs. Drugs such as calcium, [lidocaine](#), [magnesium sulfate](#), [neostigmine](#), and [sodium bicarbonate](#) are expressed as a dilution ratio or percentage. Our recommendations could probably be applied to these as well.

Medscape: Is additional research planned in this area?

**Dr. Sullivan:** We would like to implement these changes at our hospital to improve the safety of IV epinephrine use. Perhaps, if resources permit, we will be able to study the effects of these changes. We invite others to do the same.

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*Reviewed by Gary D. Vogin, MD*

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