

inappropriately prescribe levalbuterol hoping that it will reduce side effects. This is contrary to evidence from well-designed randomized controlled clinical trials [4,5] that show no additional benefit in using levalbuterol over racemic albuterol in children with acute asthma exacerbations. This study is the first of its kind to clearly demonstrate this discrepancy and the loss in translation from clinical evidence to clinical practice. Given the higher costs of levalbuterol compared to the racemic mixture [8], these misconceptions are increasing treatment costs of patients with acute asthma exacerbations.

Neil G. Uspal MD
*Division of Emergency Medicine
 Children's Hospital of Philadelphia
 Philadelphia, PA*
 E-mail address: uspalng@email.chop.edu

Dewesh Agrawal MD
*Division of Emergency Medicine
 Children's National Medical Center
 Washington, DC*

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CLEAR: Central Line Emergency Access Registry The CLEAR project protocol methods paper

The placement of central venous catheters (CVCs) is a common procedure during the assessment and treatment of seriously ill and injured patients. There is an extensive

bibliography of descriptive and observational studies of CVC placement. In recent years, research surrounding CVC placement has included such diverse aspects such as the following:

- the use of ultrasound guidance to improve success rates [1],
- complications related to CVC placement at certain anatomical sites [2],
- the importance of CVC use in septic patients [3], and
- an analysis of a closed claims database to determine complications and litigation related to CVC placement [4].

Professional organizations have created consensus documents regarding the placement of CVC, in an effort to reduce both immediate (eg, pneumothorax) and delayed complications (eg, line infection). For example, in October 2001, provided a policy statement on the use of emergency ultrasound and its use in vascular access techniques [5]. The evidence that supports these consensus guidelines is often less than robust, often due to the small sample size from one site.

In addition, we have observed several aspects of CVC placement where published information is deficient or incomplete. Examples include the following:

- an analysis of the training and supervision associated with CVC placement;
- the “learning curve” associated with CVC placement training; American College of Emergency Physicians (ACEP)
- the rate of complications associated with CVC placement using different approaches, techniques, and adjuncts; and
- compliance with consensus guidelines for CVC placement, especially in community hospitals.

For these reasons, we see the need for a multicenter registry of CVC placement to collect a large sample size. In this article, we describe the Central Line Emergency Access Registry (CLEAR) project seeks to establish a large multicenter, observational registry of data related to CVC insertion by emergency physicians in academic residency programs throughout the United States. It is our goal to recruit 15 additional academic and/or community emergency medicine programs into the CLEAR project. The online collection of data into the CLEAR database will allow us to monitor various aspects of CVC insertion by emergency medicine residents and attendings on a much larger scale.

The CLEAR registry will enroll patients in whom CVC placement is attempted. Our goal is to enroll 15 academic and/or community emergency medicine departments. Each site is required to have an annual emergency department (ED) census of at least 35 000 patients and be staffed 24 h/d with American Board of Emergency Medicine (ABEM)

candidates or diplomats. The study began in November 2005 and is currently ongoing. Inclusion criteria will be as follows:

- age at least 18 years and
- attempted placement of a CVC by an emergency medicine resident or attending physician for a patient either in the ED or intensive care unit (ICU).

The data collection tool was created, and a paper pilot was done at Maricopa Medical Center, Phoenix, AZ in [8/2005-11/2005]. The paper pilot was the basis for the online data entry fields.

Data collection for the CLEAR registry will be via an online database, www.clearsite.org, which allows for reporting of CVC placement attempts. For the initial phase of the CLEAR project, we wish to focus on those catheters being placed by emergency medicine residents or attending physicians in the ED or ICU setting, but the online registry could accommodate CVC placement by other specialties and in other hospital locations.

Physicians placing a CVC will log onto the www.clearsite.org database using their own unique password and log-in name. Participating centers will encourage online entry as close to time of catheter insertion as possible to improve accuracy of entered data variables.

After accessing the online data entry screen, physicians will be asked to enter patient variables such as age, sex, average weight (kg), and data of procedure. Patient data variables will follow an Health Insurance Portability and Accountability Act (HIPAA) Limited Data Set format, and no patient identifiers such as name or medical record number will be entered into the database. The physician will be asked to respond to a series of questions related to the CVC insertion attempt, including indication for placement, number of attempts required for successful placement, anatomical sites used, level of training, presence of supervising physician, and complications related to placement.

Collected data variables will be sent to a Microsoft SQL 2000 database running on a dedicated server that will be protected by the firewall at Maricopa Integrated Health System (MIHS), Phoenix, Arizona. Firewall, password encryption, and other security technology will be managed by the Information Technology Department at MIHS, and all patient identifiers will be scrubbed.

Each site will maintain a logbook for CVC placement attempts kept in a secure location within each ED and/or ICU. After completing the online data entry, physicians will place the patient's name, medical record number, and date of the CVC placement attempt into the logbook and verify that they have entered the required online data. Patient identifying information will be used for tracking purposes at the individual sites to verify enrollment of CVC placement attempts. The logbooks will also contain a hard copy, in PDF format, of the CLEAR data entry form in case of technical difficulties with the site or inability to access the registry. Hard copy data sheets can also be

entered by research personnel into the online database at a later time.

Each CLEAR site will have a principal investigator (physician) and a project coordinator (research staff). Project coordinators at each site will review their institution's data on a monthly basis. Project coordinators will compare CVC placement attempts entered into the CLEAR registry with at least one other site-specific source of CVC attempts, such as resident procedure logs, professional physician billing systems, hospital charging systems, CVC kit supply tracking systems, and others. For those CVC attempts identified by these site-specific sources but not noted in the site logbook, the appropriate resident or attending physician will be contacted by the site project coordinator and data collected.

Other methods to ensure compliance with data collection may include monthly or quarterly reminders sent to physicians, reminders of the CLEAR project attached to each CVC kit kept in the ED or ICU, and reminders at nursing staff meetings of this ongoing, prospective project.

Institutions will be required to meet at least 90% compliance for CLEAR registry enrollment for all CVC insertion attempts. Should institution not reach this goal of more than 90% compliance, they will be asked to withdraw from the CLEAR project.

A waiver of informed consent will be used by participating institutions because of the observational nature of the CLEAR study.

The following definitions will be used:

We defined *CVC* as achieving traditional central venous access by using the jugular, subclavian, or femoral veins.

We defined an *attempt* as one operator attempting to place a CVC at one anatomical site. If a second site or operator was needed for successful insertion, this constituted a failed attempt. Although prior studies have chosen to define an attempt as one skin puncture or single pass of the needle, we feel that our definition describes the reality of CVC insertion in an emergent setting. Even the most skilled operators may require more than one skin puncture in their "attempt" to place a CVC. We also chose to record skin punctures per attempt to determine their association with overall success rates.

We defined *placement* or *success placement* as a combination of the physician's gestalt as well as adequate venous blood return with no acute complication. An acute complication included arterial insertion of the CVC line, pneumothorax, or subcutaneous insertion, and others.

Data being entered into the online database (www.clearsite.org) will be "scrubbed" and encrypted, and all patient identifiers will be removed. Entered data will be kept on a separate server protected by firewall technology and managed by Information Technology Department at MIHS. Data will be entered into Excel databases, and statistical analysis will be performed with Stata Software (Stata Corp, College Station, TX).

Participating institutions will be able to access their site-specific real-time data and compare their results to the total of all participating CLEAR study sites. Site-specific data may

only be accessed by each institution's research personnel using a restricted "administrator" login and password. Individual CLEAR sites will not be able to access another institution's data or compare their own data to another specific institution.

The CLEAR Project Steering Committee will be formed of one principal investigator from each site. Access to the data and future study ideas will be controlled by the Steering Committee (A.B., F.L., S.J.S.).

Where appropriate, sample sizes will be calculated for comparisons using assumptions of a 2-sided α of .05 and a 1-sided β of .2. The clinically relevant difference between groups will vary according to the clinical situation. For example, a 10% absolute difference in successful placement rate comparing subclavian vs internal jugular CVC placement maybe considered clinically relevant, whereas a 2% absolute difference in line sepsis rate may also be clinically relevant.

Data analysis will be done with the assistance of statistical consultants. Because most data will be observational (not random assignment), comparisons will be done using measures of effect, such as odds ratios and absolute confidence interval differences.

Multicenter registries have proven successful for the study of a wide variety of clinical situations, from ST-segment elevation myocardial infarction to multidrug resistant *Staphylococcus aureus* skin infections. In emergency medicine, the National Emergency Airway Registry has demonstrated the potential of a multicenter study of a common medical procedure. One benefit of a multicenter project is the enrollment of large numbers of patients for a robust data set.

A multicenter observational study has important limitations as follows:

honor system,
provider variation, and
correlations and associations, not causation.

We anticipate a number of potential comparisons using the CLEAR data as follows:

1. the benefits, if any, of using ultrasound guidance for the placement of CVC,
2. the number of CVC placements needed to become proficient in their placement,
3. successful CVC placement rates based upon level of training (postgraduate year [PGY]-1, PGY-2, and others),
4. successful CVC placement rates based upon anatomical site (femoral vein, subclavian, internal jugular) in conjunction with level of training,
5. complications associated with level of training (PGY-1, PGY-2, and others) for CVC placement,
6. complications associated with anatomical site of CVC placement,
7. average number of operator attempts based on level of training (PGY1, PGY2, and others) for CVC placement,
8. average number of operator attempts per anatomical site for successful CVC placement,

9. indications for ED placement of CVC,
10. proportion of CVC placed using sterile technique, and
11. describe medications used in CVC placement.

One additional potential benefit is that the CLEAR registry will also provide a collaborative venue to improve the training and teaching of CVC insertion at residency programs around the country.

If the CLEAR registry proves that large amounts of accurate information can be collected, it may be possible to change the structure from simply observation into intervention. Such a change would require a new institutional review board consideration and probably patient consent for enrollment.

The CLEAR (Central Line Emergency Access Registry) project seeks to establish a large multicenter, observational registry of data related to CVC insertion by emergency physicians. The data will be collected prospectively and used for research purposes.

Adam Balls MD¹
Frank LoVecchio DO, MPH
Stephan J. Stapczynski MD
Mary Mulrow RN

*Department of Emergency Medicine
Maricopa Medical Center Phoenix, AZ
E-mail address: frank.lovecchio@bannerhealth.com*

Brian Levine MD
Christiana Care Health System

Ross Berkely MD
University Medical Center Southern Nevada

Ed Panacek MD
University of California, Davis Medical Center

Andrew Miller DO
Lehigh Valley Hospital-Muhlenberg

Craig Norquist MD
*Scottsdale Osborn Healthcare
Scottsdale, AZ*

Ralph Riviello MD
*Thomas Jefferson University Hospital
Philadelphia, PA*

Roy Ary MD
Emory University School of Medicine

Elliot Rodriguez MD
*State University of New York Upstate
Medical Center University*

¹ Dr. Balls is currently affiliated with SAUSHEC Emergency Medicine Residency, Wilford Hall Medical Center, Lackland Air Force Base, TX.

Janet Young MD
University of North Carolina at Chapel Hill

Eric Gross MD
Hennepin Country Medical Center

Lisa Mills MD
Charity Hospital of Louisiana-LSU

Wes Zeger DO
University of Nebraska Medical Center

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An unusual case of dipropylene glycol toxicity

To the Editor,

The recent case report published by LoVecchio et al describing renal failure with cortical necrosis and polyneuropathy after the ingestion of a dipropylene glycol (DPG) containing product highlights several of the clinically relevant limitations to timely diagnosis of the toxic alcohol-poisoned patient. This is particularly apparent when patients present late in the course of illness. Unfortunately, most health care facilities have limited, if any, capabilities to measure the toxic alcohol and their respective acid metabolites. This case describes previously unreported clinical findings after DPG exposure including delayed onset renal failure with evidence of cortical necrosis and progressive peripheral axonopathy that was persistent at 6-month follow-up.

The clinical findings in this case are eerily similar to what is known about diethylene glycol (DEG) toxicity, a toxic alcohol responsible for several mass poisonings [1-3] and commonly found in similar commercial applications, including fogging solutions. Hasbani et al [4] reported a case of acute renal failure with cortical necrosis and cranial and peripheral demyelinating sensorimotor polyneuropathy with quadraparesis and encephalopathy after the intentional ingestion of a fogging solution containing 28% DEG. The patient had a 5-month hospital course and remained dialysis dependent with residual, although improved, neuropathy. We reported a similar

presentation in a patient who intentionally ingested wallpaper stripper containing 26% DEG with acute renal failure due to cortical necrosis and demyelinating sensorimotor peripheral polyneuropathy [5]. At 6 months, our patient's neurologic function was improved, although not back to baseline, and he remained dialysis dependent. In the fall of 2006, 118 patients in Panama were treated for DEG poisoning after the ingestion of contaminated cough syrup. Patients consistently had oliguric or anuric renal failure with progressive neurologic abnormalities [2,6]. Similar to the case LoVecchio et al described, cranial nerve palsy was a common feature in the Panamanian epidemic (49.1%) and has similarly been described in other cases of DEG poisoning [1,4,5,7].

In light of the similarities of DEG toxicity with this case of apparent DPG toxicity and the propensity of this glycol to be used in fogging solutions, we wonder if DEG was considered in the differential diagnosis. Did the manufacturer confirm that DEG is not used in the manufacturing of this product? Was an aliquot of the solution available for analysis to confirm its chemical constituents? Several recent reports of adulterated products have highlighted the potential for toxicity with ingredients other than those readily identified on a product's label [8]. There is a disconnect in this case between the apparent lack of significant toxicity of DPG in animal testing and prior reports and this patient's severe toxicity. Because some of the pharmaceutical epidemic poisonings occurred as a result of DEG contamination of glycerin or propylene glycol, we wonder if this DPG-containing product was contaminated with DEG as well? This would explain his renal and neurological injuries, since these are now well-described in DEG poisoning cases. We propose that DEG should be considered in the differential diagnosis of glycol ingestions in patients with symptoms not normally expected, especially with renal failure due to cortical necrosis when accompanied by significant neurological injury.

Jamie Nelsen PharmD
Jeanna M. Marraffa PharmD, DABAT
Christine M. Stork PharmD, DABAT
Department of Emergency Medicine
SUNY Upstate Medical University
Upstate New York Poison Center
Syracuse, New York, USA
E-mail addresses: nelsenj@upsate.edu
marraffj@upsate.edu
storkc@upstate.edu

Michael Hogman MD, ACMT
Department of Emergency Medicine
SUNY Upstate Medical University
Upstate New York Poison Center
Syracuse, New York, USA
Department of Emergency Medicine
Basset Healthcare, Cooperstown
New York, USA
E-mail address: Hodgmanm@upstate.edu