Chapter 1

Imperative for Change: Adverse Sterile Compounding Events

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Introduction

It has been over 20 years since the publication of the first edition of *Compounding Sterile Preparations*.[1] One might like to think that the circumstances prompting its publication would be less the case today than it was in 1995. There is evidence to suggest otherwise.

Rationale for Pharmacy Role

Until the late 1960s, a nurse prepared doses of medications in a nonsterile environment—either in a medication room or at the bedside—for hospitalized patients for administration by the intravenous (IV) route. These doses were usually administered either in an unlabeled volume control chamber between a large volume parenteral and the patient, or by IV push using an unlabeled syringe.

One of the foundational works that charted the growth of pharmacy practice in the hospital setting was *Mirror to Hospital Pharmacy*. Published in 1964, recommendations for the expanded role for hospital pharmacists were made based on a national audit of pharmacy practices. One recommendation was that "hospitals be encouraged to assign to pharmacists the responsibility and to provide for the preparation and quality control of sterile medicinal products produced in hospitals."[2]

Following the publication of *Mirror to Hospital Pharmacy*, problems with the safety of IV drug therapy were reported as a justification for pharmacy-based programs. Patterson et al. expressed concerns about drug incompatibilities and the length of time between preparation and administration of medications prepared at the bedside after finding that 60% of IV fluids used at their hospital contained more than one drug, and many were administered more than an hour after preparation.[3] These authors recommended that the pharmacy assume responsibility for compounding IV admixture doses to resolve these problems.

Flack et al. reported requests for "technical help from the pharmacy service" by the surgeons investigating the effectiveness and safety of parenteral nutrition to resolve

problems of contamination and incompatibilities with the formulas that were being "hand mixed in open laboratory surroundings."[4]

Thur et al. observed nurses preparing parenteral admixtures in patient care areas and reported an error rate of 21%. The rate of wrong doses prepared was 9%, incompatible drugs mixed was 6%, wrong drug or solution used was 3%, and preparation of drugs not ordered was 3%. Deviations from accepted sterile technique were observed, with counters not being cleaned (99%), hands not washed (97%), touching sterile areas of the IV container (47%), and vial or bottle tops not being cleaned (31%).[5]

O'Hare et al. used a disguised observer method to evaluate physicians' and nurses' errors in preparation and administration of IV medications. They found that physicians made at least one error in 98% of the doses prepared and 83% of these doses were administered by nurses.[6]

Taxis and Barber also observed nurses who prepared and administered IV drugs on 10 wards in a hospital in the United Kingdom. Of 249 errors identified, at least one error occurred in 212 of the 430 doses observed. Most errors occurred when bolus doses were prepared and administered or for doses requiring multiple preparation steps. One strategy recommended for decreasing errors was to reduce the amount of preparation on the ward.[7]

Even if properly ordered, errors can occur in preparation. Thompson et al. evaluated the concentrations of admixed medications delivered to patients and found evidence of incomplete mixing of medications in IV solutions prepared at the bedside. They also found that there was more uniformity of concentrations of potassium chloride when these doses were prepared in the pharmacy.[8]

Calculation errors are also a root cause of error in preparing medications. Perlstein et al. found that one of 12 doses calculated by nurses had an error, which resulted in a tenfold dose compared to that ordered. Pediatricians made errors in one of 26 computations. Pharmacists made fewer errors than nurses and physicians.[9]

Although these studies provide a historical basis for the pharmacist role in compounding sterile preparations, a recent systematic review and meta-analysis of the risk of microbial contamination of parenteral doses (prepared under aseptic techniques in clinical and pharmaceutical environments) remind us of the risks associated with compounded sterile preparations, particularly when they are prepared in the clinical environment.[10] In a review of 16,552 doses from 34 studies for all data combined, a significantly higher frequency of contamination of doses prepared in clinical settings was found than in pharmaceutical environments. Contamination of doses was significantly higher when prepared as individual lots than as part of a batch in pharmaceutical environments. The authors concluded that reported rates of parenteral dose contamination were orders of magnitude higher than accepted reference standards and may increase infection risk, and the data supported dose preparation in pharmaceutical rather than in clinical environments.

Self-regulation

As a result of these reports, pharmacy-based, centralized IV admixture programs emerged as a potentially safer medication-use system. According to ASHP National Surveys of Pharmacy Practice in hospital settings, this system is present in the vast majority of U.S. hospitals. By 2008, only 10% of U.S. hospitals relied on nurses to prepare IV medications as the primary method. Most hospitals use the minibag system to administer medications by the IV route, and doses are prepared in the pharmacy.[11]

Twenty years after adoption of pharmacy-based IV admixture programs, reports of patient harm resulting from improperly compounded sterile preparations began to be published. In 1990, four deaths resulting from contaminated cardioplegia solutions prepared in a hospital were reported.[12] In the same year, several infections and cases of blindness were traced to ophthalmic preparations compounded in a community pharmacy.[13] Under pressure from the U.S. Food and Drug Administration (FDA) to strengthen their oversight of pharmacist compounding of sterile preparations, ASHP began a multistep plan to assist its members to improve practices. The first step was to convene an invitational conference in 1991 to discuss quality assurance for pharmacy-prepared sterile preparations.[14] A *Technical Assistance Bulletin on*