Medication Errors or Drug Errors in Anesthesia. (2018-8-18)

Dr. Robert Raw MD
MBChB, MFGP, MPraxMed, DA, FCA
Professor of Anesthesia retired
Editor of Regional-Anesthesia.Com

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1. INTRODUCTION

Medication errors harm patients. Medication errors can cause death or permanent injuries. The true incidence of medication errors with anesthesia is unknown for two reasons;

(1) Voluntary reporting is dependent on the care provider (anesthesiologist) actually *realizing and knowing* of the medication error he or she made, and
(2) Voluntary reporting requires the care provider (anesthesiologist) being 100% *honest and revealing* all of the errors.

Therefore, the true incidence of anesthesia associated medication errors is certainly much larger than that ever measured. The magnitude of the true problem is additionally concealed by the fact that many medication errors may not produce a single discernable consequence. That last fact however, does not diminish the overall seriousness of medication errors.

Pediatric anesthesia is particularly a risk area for medication errors due the fact that many drugs have to be diluted before administration[1]. That can double error rates.

The remedies and strategies to prevent the problem may seem conceptually simple, but they generally yield disappointing results. Burdensome and complex strategies to eliminate medication drugs errors, have never eliminated medication errors and often these strategies have their own unanticipated secondary consequences.

Medication Errors are also called Adverse Drug Events (ADEs), or drug errors, with each author having very slightly different definitions.

This presentation is hoped to provide the anesthesiologist with some very simple strategies that could help moderate their own medication errors.

2. OBJECTIVES OF THIS PRESENTATION;

After studying this material, the reader should;

- Be *obsessed* about avoiding anesthesia medication errors.
- Believe that he or she will make a medication error *once out of every 133* times they administer a drug.
- Believe he or she will make a medication error *once in every 10 anesthetics* they provide.
- *Read the drug label* every time they handle a drug or a fluid.
- *Read the syringe label* every time they handle a syringe containing a drug.
- Voluntarily *report every error* they realize they made to an appropriate authority.

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3. CONSEQUENCES OF THE DRG ERRORS.

Patients may be harmed by;

(1) *Failure to achieve therapeutic benefit* due to the omission of the correct and intended drug.

(2) *Pharmacological by side effects* of the drug given in error. The pharmacological side effects can be extreme and even bizarre if an administration route error introduced the drug direct onto tissues that would more normally only be exposed to that same in dilutions of 50 000 times or so.

(3) *Chemical effects* can occur direct from the error drug if it meets tissues in extremely high concentrations. Chemical effects can be tissue toxic. Chemical effects tend to destroy cells and tissues.

(4) Chemical effects can also *alter the bioavailability of other drugs within a* solution and affect their solubility if that is sensitive to pH changes. That will secondarily alter the pharmacological effects of the second drug. This class of problem occurs when solutions are altered by dilution or use of additive drugs.

The commonest consequence is nothing observable. The worst outcomes are death or permanent tissue damage. The patient may also altered costs, and altered duration of stay in hospital. Choi studied costs of drug errors in general hospitalized patients in South Korea in 2016[2]. Choi estimated an average added cost of about $US8000 to treat the consequences of the drug errors identified.

4. CASE EXAMPLES OF DRUG ERRORS.

Published case reports of medication errors do exist, but are few in the literature and they do not indicate the incidence of medication errors. Published medication-error cases insufficiently illustrate the seriousness of the problem and the magnitude of the problem. The following cases are from the author's personal experience, or from the experiences of persons he has communicated with personally and discussed their cases with.

1. **Death after spinal anesthetic medication error**; A patient underwent spinal anesthesia. The block did not set up well and general anesthesia was needed. After surgery and awakening from general anesthesia, the patient developed strange neurological symptoms that steadily progressed up the trunk over 36 hours, eventually requiring the patient be intubated and ventilated in an intensive care unit where they died five days after surgery. At the end of the initial surgery a full 5 ml syringe of local anesthetic was found and an empty 5 ml syringe of alcuronium. The best explanation that many discussants of this GASNET case is that the alcuronium (non-depolarizing muscle relaxant) had been injected intrathecal in an <u>accidental drug swop</u>. Alcuronium is a highly polarized molecule not able to cross into the central nervous system via the blood brain barrier usually after peripheral injection. As much it cannot be metabolized in the central nervous system. Therefore its consequences persist unusually LONG. It was, likely in this case, injected within the central nervous system during the spinal block. It thus bypassed the blood brain barrier. It was unable to diffuse out of the central nervous system and persisted in its presence. It slowly redistributed from the lumbar intrathecal region towards cephalad and the brain. Alcuronium is capable of blocking many receptor types, especially in higher concentration and also of blocking some central receptor types not found in the periphery, where it is more normally injected.
2. **Injection of 200mg Ropivacaine via a central venous line.** The anesthesiologist was preparing an infusion bag for an epidural infusion and had in his hand a syringe containing 20 ml of 1% Ropivacaine (local anesthetic drug). He inadvertently injected the entire contents of the syringe into the patient's central line. He immediately realized the error while looking at the empty syringe in his hand. Nothing happened. It is possible the presence of sevoflurane volatile anesthetic altered the responses a patient would be expected to make when injected the same drug and the same fashion while awake.
3. **Injection of 100mg of morphine via a peripheral venous line.** The anesthesiologist was preparing an infusion bag for a Patient Controlled Analgesia (PCA) device and had in his hand a syringe containing 100 mg of morphine. He inadvertently turned to the patient under general anesthesia and injected the entire contents of the syringe into their peripheral IV line. The mistake was realized immediately with the empty syringe still in the anesthesiologist's hand. The patient required a Naloxone infusion for 36 hours after wards.
4. **Injection of 120 mg Ropivacaine (12 ml of 1% solution) intrathecal.** A first anesthesiologist had placed the epidural catheter 5 hours earlier. It had provided

excellent analgesia for second stage obstetric labor although the blood pressure had fallen bit more than usual. The patient later required a Caesarean section. A second anesthesiologist was called and they inject 120 mg Ropivacaine (12 ml of 1% solution) to upgrade the epidural block from a low-grade analgesia block to a high-grade surgical block. The anesthesiologist shortly noticed the patient silently mouthing the words "I can't breathe". A total spinal block was instantly diagnosed and the patient intubated and rendered unconscious under general anesthesia. After delivery of the baby arrangement was made for the patient to be transferred to an intensive care unit for continued ventilation until the local anesthetic effects wore off. The anesthesiologist, during a lull in activity after the baby was delivered decided to repeat the epidural catheter aspiration test. At first, aspiration yielded nothing. When the amount of suction was reduced a trickle of fluid returned into the syringe. By maintain minimal suction clear fluid was slowly aspirated until 36 milliliters had been removed. The aspiration was ceased at this point. As this was three time the volume injected it was considered the catheter was unequivocally intrathecal. At 60 minutes after the big epidural top-up injection, while transferring the patient to intensive care the patient brought up their hand and grabbed the endotracheal tube and self-extubated. It is likely the epidural catheter had been intrathecal ab initio but had escaped recognition of its position due to the small amounts of drug injected for labor analgesia. Furthermore, the large amount of cerebrospinal fluid that had been removed from the lumbar thecal sack had removed most of the ropivacaine thus explaining the very short duration of the total spinal block. The lessons are; (1) when a wrong drug is injected intrathecal strongly consider doing a generous subarachnoid CSF drainage procedure which may be able to also remove most of the injected drug, and (2) when testing an epidural catheter for possible subarachnoid placement do the aspiration test with minimal suction and with patience.

5. **Criminal intentional drug swop incident.** A trainee anesthesiologist was managing an awake surgery patient under peripheral nerve block. The attending anesthesiologist entered the operating room to relieve the trainee for a refreshment break. The trainee had induced general anesthesia in the attending's absence claiming the patient had responded to surgery and had needed to be put to sleep. In addition, the patient was showing systolic blood pressure spikes to 200mg Hg every 15 minutes which the trainee treated with a dose of 100 microgram of fentanyl. The attending said he would observe the patient and sent the trainee out. The patient subsequently maintained a perfect blood pressure not requiring any medications. The recorded chart showed a tram line straight track of near identical blood pressure recordings in the next hour which starkly contrasted to the spiky up and down record of the preceding two hours. The record was a written paper record of 15-minute interval vital sign recordings. The attending anesthesiologist was intrigued and also examined the anesthesia machine digital record of the case. It did match the paper record. The trainee returned and took over the case. After the completion of surgery, the attending anesthesiologist returned to the operating room and noted that when the patient was again under the trainees care the high blood pressure peaks had returned, and the again it was treated with fentanyl. Despite (presumably) receiving a vast amount of fentanyl, and serial blood pressure

recordings of 200 mg Hg the patient woke up immediately and had a fully functional nerve block. It was later realized the trainee had periodically injected the patient IV ephedrine to induce the high blood pressures, to create an excuse to administer the patient fentanyl. The trainee subsequently was discovered to be a fentanyl addict and diverted to himself all the fentanyl he recorded as administered to the patient. The high blood pressure spikes the patient had every 15 minutes were secondary to injected ephedrine that the trainee did not make a record of. The patient did well despite this chemical assault. The trainee went into an incarcerated drug rehabilitation program. Key point; consider a medication error when patient vital signs, or patient responses or patient outcomes seem bizarre and are inexplicable. Had this story been better understood at the time, the trainee would also have been charged with attempted murder of the patient as well, in my opinion.

6. **Wrong dose medication error**; for a modestly low blood pressure an anesthesia provider gave a patient an IV phenylephrine bolus meant to be 50 µg. The blood pressure shot up to 300 mm Hg systolic pressure. A while later when a low blood pressures again occurred was again treated each time with a supposed dose of 50 microgram phenylephrine and the blood pressure again spiked at 300mg HG systolic pressure each time. When this bizarre pattern was analyzed it was realized that the phenylephrine syringe that had been used to inject undiluted phenylephrine into a 250 ml bag of normal saline, was then immediately refilled with presumed diluted phenylephrine. The bag of saline had not been agitated and shaken to mix the drug evenly before it had been aspirated for the diluted drug. The dilution exercise was repeated by the trainee using methylene blue and the pattern of blue dye spread was observed between a shaken bag and an unshaken bag, and the syringes of “diluted methylene blue” drawn from each bag. The two syringes when viewed side to side had a major color difference and at a guess the darker blue syringe had 20 times the methylene blue than the syringe drawn for the 250 ml bag of methylene blue that had been shaken and agitated before withdrawing the dye. It was then presumed the first syringe of supposedly dilute phenylephrine had contained a drug concentration likely equally about 20 times higher than that it was meant to contain.
7. **Johannesburg Anesthesia Dinner Discussion Club (JADDC)**. This was a fortnightly meeting, convened by this author for 10 years up to 2004, amongst private practice anesthesiologists. The format involved a short lecture and short case presentation and much open discussion. In addition, a meal and alcohol were consumed and there was good camaraderie. When a recognized critical drug substitution error was ever discussed, it was notable that close to all of the attendees would confess during discussion to having also made drug substitution errors in the same year. Cases discussed included patients dying immediately upon induction of anesthesia due to thiopentone being reconstituted with KCl solution instead of Na cl solution. This particular medication error was a near annual occurrence within the metropolis of 7 million persons, until thiopentone became replaced with the pre-mixed propofol in popularity.
8. **Injection of nerve block with muscle relaxant drug[3]**. A seventy-nine-year-old lady had 50 mg of atracurium muscle relaxant injected onto her axillary brachial plexus. Two

minutes later she became dyspneic and paralyzed. The drug error was identified. General anesthesia with airway management was initiated. She finally recovered fully without nerve injury.

9. **ICU nurse injects an antibiotic via the arterial line**. The patient ended with a forearm amputation. The nurse continued to deny having made an arterial injection. The circumstantial evidence and time sequence of events were however condemning. The hospital made an out of court settlement to the patient.
10. **A patient received an interscalene block with 0**.5% bupivacaine diluted to 0.25% with normal saline by the anesthesia assistant. The patient lost permanent function of the entire brachial plexus from C5 to T1 in that side. The skin over the point of plexus injection sloughed and had to be replaced with skin grafts. This was the consequence of the bupivacaine having been diluted with Calcium chloride (CaCl) by error instead of sodium chloride (NaCl). Both the fluids ampules of CaCl and NaCl had identical sizes and color labels at a glance. The drug cart container had been mistakenly replenished with CaCl ampoules instead of NaCl ampoules. The anesthesia assistant had read the NaCl storage container only and not the actual label of the ampule taken from the container. Calcium chloride is highly tissue toxic when injected direct into tissues. It caused the necrosis of the plexus and overlying muscles and skin.
11. **An interscalene block was performed using ultrasound guidance and 0.5% bupivacaine with clonidine was injected[4].** The patient also had multiple sclerosis. The injections were well documented on ultrasound images, to be extra-neural to the upper trunk. A needle-based or mechanical injury is thus a very unlikely mechanism for the injury. Good postoperative care excluded a hemorrhagic mechanism to have injured the plexus. Furthermore, the safety of peripheral nerve block in the presence of multiple sclerosis is documented, so that excludes the underlying disease as being dominant factor. Clearly, this very wide a field of nerve injury suggests this is most likely a chemical injury from a drug error injected in a large volume. Clonidine is manufactured in a 10 ml ampule with a green top and green ink labels. The list of alternative drugs that all had 10 ml size ampules, green pop-off tops and green ink labels were dozens. The two drugs it is thought that were most likely to have been possibly mistakenly placed in the anesthesia cart and mistakenly added to the nerve block injection drugs instead of clonidine was metoclopramide or a chemotherapeutic drug used intra-surgical sometimes. The use of the intended additive clonidine was not critical to the case. Avoidance of additives to the local anesthetic solution would have avoided this nerve injury.
12. **An interscalene block was performed using ropivacaine after diluting it, and permanent nerve injury resulted[5]**. The case report states "no additives" were used. They overlooked the fact that they diluted ropivacaine from 0.75% to 0.6%, supposedly with 0.9% sodium chloride (NaCl). One co-author reported privately that using 0.6% ropivacaine was the preference of the senior teacher on the case the trainee would prepare the dilution hastily shortly before the nerve block was performed. Two days after the nerve block the patient developed most severe shoulder girdle pain, with allodynia and a permanent deficit of the axillary nerve. Although the picture is partly suggestive of the patient developing complex Regional Pain syndrome (CRPS) the more

likely event was that drug substitution error was made with the hasty diluting of the original nerve block solution. The unknow error-solution affected the posterior division of the brachial plexus onto where it was injected directly, worst. One should regard dilutents as drugs and verify the dilutent ampule with the identical ritual safety procedures, as for any other drug used.

5. REVIEWS ON DRUG ERRORS.

The commonest outcome of a medication error is nothing. The patient however may experience lack of benefit from not getting the intended drug.

Dhawan reviewed drug errors in anesthesia in 2016[6]. Dhawan estimated an anesthesiologist would inject 500 000 drugs across his/her career. Assuming the “Webster incidence” as correct that would mean well in excess of 4000 drug administration errors would be made. The consequence of any one drug error could span a spectrum of events ranging from nothing to death. Even if a wrong drug was injected with no direct effect, it can be argued the patient was at the least deprived of the benefit of what the correct drug could potentially have induced. One death ever however, is a tragedy to be maximally strongly sought to be avoided. Dhawan determined that the wrong drug was injected in 48% of anesthesia drug errors, the overdose dose of drug in 42% of cases, the drug was injected into the wrong site in 8% of cases, the drug was injected in an inadequate dose 4% of times, and the drug was omitted in 2% of cases. When a wrong drug was injected the error lay in using the wrong drug ampule in 33% of cases, and using the wrong syringe in 17% of cases. When an overdose occurred, in 53% of cases the error was due to an intellectual deficit, a pump setting mistake occurred in 21% of cases, and a dilution error in preparing the drug in 5% of cases. Dhawan noted that a drug error could occur during (1) drug preparation, (2) during drug administration or (3) during recording of the drug. An error of recording may possibly conceal that a correct drug was correctly administered and thus become a **false drug error** in retrospect. Equally an error in recording may reflect the correctly intended drug and dose that should have been administered, and thus **conceal the error** that actually occurred.

Cases are also known to this author, where trainee drug errors were intentionally recorded different to that which was administered in order to conceal the drug error made. That event related to opiate diversion to serve the trainees drug addiction. This is likely not an unprecedented type of action. Many of these latter type of facts, make the study of drug errors very difficult.

Llewellyn from South Africa in 2009, determined 40% of identified drug errors resulted purely from misidentification of drug ampules during drug preparation. That is, the person aspirating the contents of the ampule into the syringe did not read the drug ampule label.

Cooper identified risk factors for when anesthesia drug errors more likely occur[7]. Inexperience as an anesthesiologist was blamed in 16% of cases, unfamiliarity with the drug pumps was blamed in 9.3% of errors, haste was blamed in 6% of errors, and being distracted or inattentive in 6% of drug errors.

Medication errors leading to medico-legal claims, have amongst the highest risk of a successful claim with highest payouts being awarded[8].

6. CLASSIFICATION OF DRUG ERRORS.

Drugs errors can fall into two broad group types each with subcategories. The groups are; (1) recognized drugs errors, and (2) unrecognized drug errors.

Unrecognized errors are a big problem in part because they are likely the greatest portion of drugs errors which makes studying them very difficult, and in part because their consequences can be attributed to other, innocent drugs or interventions leading to inappropriate altered medical care of unrelated events to that of the drug error.

Drug errors can occur at the manufacturer wrongly packaging, labeling or pharmaceuting or manufacturing a drug. This is a rare problem but unfortunately still an annual ongoing problem around the world. Appropriate over sight by authorities can minimize that problem. For today's discussion we are mainly looking more at the level of the anesthesiologist who personally administers drugs to patients. Anesthesia providers are unique in that they have to prepare the drugs, repackage the drugs to a different container and also administer the drug via parenteral route mostly.

In the anesthesia context, drug errors can be classified as

1. SYRINGE SWOP. This error occurs when a correct drug is decided to be used, but a wrong drug is actually administered from a syringe correctly labeled for the contents. That is, the syringe contents match the label. The errors arises from not reading and comprehending the syringe label before administration. This is common.
2. SYRINGE LABEL ERROR (Drug swop). This error occurs either when a syringe is either (i) filled with the correctly intended drug but is mistakenly wrongly labeled at its time of preparation, or (ii) the syringe is correctly labeled as with the intended drug content but is filled with the content of a wrong drug ampule. At a later time that drug gets administered as per the label but a different drug is actually injected to that intended. This is common.
3. AMPOULE LABEL ERROR. This error occurs at the factory or in the pharmacy making prefilled syringes. The factory produces an ampoule where the label and content do not match. The anesthesiologist can do nothing to recognize this other than report inappropriate patient responses. This is rare, but is recognized by widespread reporting of inappropriate patient responses to injected drugs. This is rare, but not unheard of.
4. DRUG PACKAGING ERROR. This occurs at factory level, and at hospital pharmacy level where drugs are repackaged into containers for the anesthesia drug cart. This is very rare. The ampules are correct for content as ampule-labeled, but are stored in wrongly labeled package boxes as a group.
5. DRUG REPACKAGING ERROR; This occurs in the operating rooms when anesthesia drug carts are restocked and incorrect drug ampoules are stored in labeled storage compartments or containers. The first remedy is to always read the ampoule label after removing it from its storage space, apart from reading the container label. Reading the storage label to find the drug is not the same as reading the ampoule label to use the drug. This is a very common error.

6. PHARMACEUTING DILUTION ERROR. This is mainly a final user's error of diluting the drug incorrectly.
7. ADMINISTRATION ROUTE ERRORS. A patient may have injection tubing to an arterial line, a venous line, a central venous line, an epidural line or peripheral nerve block line. It has happened that drugs intended for one line were inadvertently injected into another line. Consequences range from simple failed therapy to permanent tissue loss of or even death. This is a particularly serious type of error.
8. PHARMACEUTING ADDITIVE ERROR. This is mainly a regional anesthesia problem where it is popular to added components to local anesthetic solutions to augment their effects. The consequence of adding an incorrect drug may only be apparent at a time well after the anesthetic thus making retrospective recognition of the drug error usually impossible. In addition as the drug is injected direct onto target tissues before any drug dilution occurs in the body's full blood volume. This creates the potential for the drug to be tissue toxic via *chemical effects* on nerve tissue. This make avoiding this class of medication errors even more urgent. It is a strong reason to eliminate use of local anesthetic additives.
9. COMMUNICATION MEDICATION ERRORS. This occurs when one person administers a drug under direction of another person. An additional third person may be recording the drug administration and may make a recording error. When the team is multi-ethnic or multi-cultural with differing accents, or familiarity with different terminology from having trained in another institution may lead to the mishearing of instructions. Drugs with similar names may easily be misheard.
10. EQUIPMENT MEDICATION ERRORS. This large group of errors will not be discussed in this presentation. This includes use of infusion pumps.
11. WRONGLY RECORDED MEDICATION ERRORS. The advent of electronic medical records and electronic medical ordering has added the errors of wrong selection of a drug or dose or time or a route off a drop down selection list. Review of documented EMR record drug errors suggest that in many cases the correct drug was likely given and only it was wrongly recorded. This invites speculation that as many recording errors are made for correctly administered drugs, as there must be actual drug administration errors concealed by the recording of the drug that would have been correct and that was the intended drug to be administered.

The relative frequency of medication error type in one study showed giving the wrong drug from a correctly labeled syringe was the most common mistake[9]. This was mainly due to misidentifying the drug ampoule at the time of preparing the syringe. Next most common problem was misidentifying the syringe at the time of drug administration, and this correlated with mixing up syringes of identical size especially 2 ml syringes. The most common drug involved in a medication error was a muscle relaxant drug. Another risk factor was miscommunication when two and more persons were simultaneously managing the anesthetic.

7. INCIDENCE OF ANESTHESIA DRUG ERRORS

Drug errors occur in all fields of medicine. The incidence of general medication errors represents the cause of 3.7% to 16.6% of all general hospital admissions[10,11]. It is certain that all reported drug errors only partially reflect the true drug error rates. In non-anesthesia hospital settings where the family spend near 100% of the time with a hospitalized patient medical errors have been studied[12]. In that study the family was solicited to report medical errors, as they perceived them to be. The family reported rates of medical errors were 500% higher in incidence than what the prior physician reported incident rates were. It is thus likely that anesthesia provider (physician, assistant, and nurses) reported drug error rates are also under-reported.

Webster did a prospective study which suggested medication errors occur in 1 in every 133 interventions or injections[13]. This is considered the single most credible study on the subject and the "*Webster rate*" of anesthesia drugs of 1 in 133 drugs administered is accepted as the gold measure. It is also recognized that the totally true incidence of anesthesia drug errors is higher, but impossible to determine to this present date with existing technology.

Hausman report at the 2016 ASA conference of a multihospital University of Michigan review of anesthesia drug error reports. The reports were voluntary and out of 434 554 anesthetics and drug error rate of 1 per 2000 was reported. The Webster rate would be 15 per 2000. That suggest extensive voluntary underreporting of drug errors. Antibiotics were the most common drugs reported about. The most common factors in the error were judgment errors relating to allergies, and accidental syringe swops. Hausman speculated under-reporting was driven by fear of punitive action against the anesthesia provider.

> The 2016 study by Nanji has been much quoted although the error accuracy described is highly doubted[14]. The definitions of drug error are extremely "soft" and somewhat bureaucratic. The described incidence of 1 in 20 errors occurring with drug administration thus is highly exaggerated. Some events counted were only potential errors detected prior to administration, and thus not drug administration errors at all. Some events counted were trivial administrative failures, but with correct patient care actually having been given.
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> Zhang, with Webster, in China, 2013, reported an anesthetic drug error rate of one in every 92 anesthetics[15]. If 7 drugs are injected per anesthetic, on average, the drug error rate is one per 645 drug administrations. The study was dependent on voluntary reporting and the rate is likely very under-reported. The study however strongly validates that a significant number of drugs errors did occur in the study hospital.

Saito, in 2015 in Singapore, initiated a no-blame highly-encouraged voluntary system of critical incident reporting in anesthesia[16]. That revealed one critical event in every 119 anesthetic cases. Of those 379 incidents 14.5% were drug administration errors. The drug error rate alone would be 1 per 793 anesthetics. It was recognized that the induction period of anesthesia was the peak time for drug errors to occur. Of all the categories of critical events reviewed drug errors was the foremost one associated with **human factors**. At the time of the drug error the anesthesiologist was likely multitasking, or inattentive due to distraction. The authors were sure their results were lower than what really occurred due to underreporting. They speculated that underreporting was due to concern for disciplinary action, lack of concern for the problems, or lack of belief in the value of reporting critical events. They believed drug errors were related to human factors, that were identifiable, predictable, repetitive, and susceptible to efforts to improve upon. Improvement could only be started from after drug error reporting. They strongly encouraged a double pronged effort in dealing with drug error reporting, namely; (i) making reports as anonymous as possible, and (ii) developing a culture of openness within a blame-free environment.

Medications errors are common in anesthesia care occurring in at least 1 in 10 anesthetic cases when prospectively studying solicited but voluntarily submitted reports[17]. Amazingly other studies report only a 1 in 5000 anesthetics drug error incidence when investigating only adverse event outcomes in anesthesia[18]. Another Thai group found that drug errors formed only 4% of all anesthesia adverse events in a 2008 study, and a third group found medication errors 9% of all anesthesia adverse events in a 2011 study[19],[20]. The peak time for drug errors was during induction of general anesthesia and most commonly involved muscle relaxants. A Japanese retrospective study of anesthesia related incidences yielded a medication error rate of 1 per 1300 anesthetics[21]. The most common error was a syringe swop most commonly involving opioids and cardiovascular drugs. The rate was unchanged over a 15 year period and risk factor was having very little anesthesia experience. Clearly the calculated incidence of anesthesia medication errors varies very widely depending on how data is primarily gathered. Prospective voluntary reporting yields highest medication error incident rates, rather than data extracted from adverse event investigations only.

A solicited voluntary self-report survey of obstetric anesthesiologist observed 70% of respondents had made a known medication error in the preceding 12 months and 40% had made more than one error[22].

This author once did an open meeting survey of about 300 anesthesiologists and about 100% of the audience raised a hand admitting to knowing of an anesthesia drug error having occurred in the preceding 12 months. That error was either by their own hand, or by the hand of a colleague who had shared a story of their own anesthesia drug error.

8. CAUSES OF DRUG ERRORS.

It has been wisely said that anesthesiology is a “Stiff” profession. For 98% of the time the anesthesiologist is *bored stiff*, and for 2% of the time she/he is *scared stiff*. The air-flight analogy is that one has hours of smooth flight above the clouds followed to very bumpy ride down through clouds and winds to land on a short runway in the middle of a mountain region. One may more likely make an error during a critical time when many things are happening simultaneously than when everything is steady and safe.

Distraction is major cause of drug errors. Distraction makes it a lot more likely that a wrong drug ampule will be drawn into the syringe. Distraction makes it more likely that a wrong syringe will be picked y up to inject from. Distraction makes it more likely one will make wrong drug decision.

An Anesthesia Patient Safety Foundation (APSF) meeting reported in 2017[23]. A variety of distractions were listed.

- Patient care related. A lapse in vigilance could develop, for example, during intra-operative use of a transesophageal echocardiogram.
- Technology related. When technology fails, as is more likely as we use more technology that can distract one. Also increasing use of computers at the patient inside have created excessive data entry requirements. Currently documenting what one does take

precedence over what one is doing to the patient. There should be clear concept of "*Treat the patient FIRST. Document the treatment second*".

- Noise and alarm distractions. Up to 99% of alarms do not need patient attention and result in alarm fatigue. With alarm fatigue one responds too slowly or not at all to an alarm. Responding continuously to false alarms distracts one when preparing and administering drugs. One may realize in the middle of administering a drug that an alarm is false and not in need of immediate cancellation, but the surgeon may pressure one to divert a hand to cancelling the alarm first, and thus worsen the distraction during drug injection. It is thus easy to inject too much or too fast, or pickup a wrong syringe.
- Interpersonal dynamics. Detrimental hierarchical gradients, and disruptive behavior by persons acting out inappropriate assertion of authority. It is usually the surgeon acting in such a fashion, often during a critical anesthesia period.
- Personal distractions. This can be from getting too deep into paper reading matters, or using personal electronic devices, or use of the operating room computer. The remedies here are not simple as elimination of such items creates negative consequences in itself.
- System related.
    - Color coded syringes. Color coded syringe labels are used where all different drugs within one class are coded with one bright color tag. The postulate is that errors will likely be confined to within the color class, and will be safer error than cross class error. That is unproven. There is strong opinion and anecdote that use of color coding discourages actual reading of syringe labels, and can this increase the incidence of drug errors.

Suggested APSF remedies from inappropriate distractions included; (i) having a "sterile cockpit on approach" period. That is other staff must refrain from being bossy or argumentative with the anesthesia team during critical periods like the induction of the anesthetic. Good surgeons ask politely "May I lift the leg?", or "May we prep the abdomen". Bad surgeons demand "Give the antibiotic now!" while one is keeping an eye on the marginal blood pressure and oxygenation while trying to insert an arterial line. (ii) Have a policy regarding type and volume of music played during surgery. One orthopedic surgeon who this author worked with used very loud heavy metal rock music when he operated with a hangover. It was good, in that it assisted the surgeon focus on the surgery and avoid unnecessary trainee questions or social dialogues. It was bad in that it made it hard to hear the anesthesia monitors and alarms. (iii) have work systems that help anesthesiologist not work when exhausted, hungry or sleep deprived.

SUB-VOCALIZING WORDS, RECOGNIZING WORDS AND THEIR LINK TO DRUG ERRORS.

There are a number of types of reading of sentences involving three levels of learned skills;

(1) Literal comprehensions. This involves identifying an event within a sentence.
(2) Inferential comprehension. This involves identifying a meaning within a sentence.
(3) Evaluative comprehension. This involves judging a situation contained within a sentence.

In order to comprehend anything in a written sentence there are two processes involved during reading. The first is SUB-VOCALIZATION (SV) and the second is SINGLE WORD RECOGNITION. These two phenomena are different yet closely linked. They can both be studied in cognitive psychology.

During anesthesia care a sentence may only constitute a single word, as in a drug label.

Sub-vocalization is the process of saying a word silently within one's head when reading it. This SV is physiologically measurable in signs of minor muscle activity using electromyography of the larynx and the tongue. With speed reading like scan-reading or skim-reading, SV is suppressed.

Sub-vocalization, when present during reading of a word helps; (i) recognize the word, (ii) comprehend the written word, (iii) and recognize the written word. Sub-vocalization is suppressed during reading when one has learned how to speed read. Most person who are intelligent above the population mean and who are educated, can speed read in some degree. Sub-vocalization is suppressed when one is distracted. Lack of sub-vocalization when reading a drug label increases the chance one makes a reading error of the label, mistaking it for another drug label.

Word recognition is done by studying the letters of a word. The word may be recognized based on seeing single prominent letter in a particular position within a word of a particular shape or length. When sub-vocalization is absent word recognition can be erroneous.

Furthermore, when one has an expectation of finding one word to read before one even reads the word, as drug label, and one is rushed and distracted, it is very possible to have zero sub-vocalization and make a word recognition error in reading a drug label.

These physiological and psychological phenomena underly the mechanisms of how some anesthesia drug errors are made.

The remedies are to minimize distraction and maximize sub-vocalization when reading labels. That is very simple – just quietly read the label aloud to yourself. Do this as a 100% routine whenever you pick up an ampule, or filled syringe, or at the moment of injecting any drug.

9. HOW TO PREVENT DRUG ERRORS - DEPARTMENTAL AND SYSTEM MANAGEMENT STRATEGIES[24]

Acquiring ongoing data on medication errors is the starting point. Each case reported must be individually studied to identify avoidable risk factors for the future. Cases should be grouped in order to detect trends and patterns. Where possible remedies must be aimed at system changes. When necessary, remedial action must be aimed at an individual.

In rare event criminal prosecution of a willfully negligent individual making a medication error with serious consequences to the patient, may be appropriate. A sporadic medication error by a well-intended good hearted individual should not be criminally prosecuted. There is much philosophical and ethical matter here for debate.

Gathering data and event reports is however the most important thing to achieve. Voluntary reporting is by its nature very limited in its success. The reporting individual reporting a personally made error runs the risk of job loss, status loss, and even freedom loss. Consequently the more successful large surveys of medication errors relied entirely on ANONYMOUS reporting. Anonymous has the very big advantage of soliciting more medication error reports, due to protecting the individual making the report. Anonymous reporting should be protected in law to make those reports protected from discovery by any legal processes. The one disadvantage of anonymous reporting is that analysis is very limited by lack of access to full records, lack of access to the individual involved for more subtle information, and a dependence on the individual reporting to select the best information reported.

Managers can be anesthesia department heads, organizational executive officers or even national governing politicians. System errors corrections can be made at many levels; (i) nationally mandated drug packaging and preparation changes for drug managers, (ii) Hospital changes in policies, and (ii) anesthesia departmental or group changes in drug handling protocols. It is critical that anesthesia providers be partners in the process of minimizing medication errors. The process starts with willing reporting of medication errors. All anesthesia associated bad patient outcomes and anesthesia critical events need review in order to identify when medication errors were likely causes. A systematic reporting back of data gathered should be made to anesthesia providers.

One study by Armitage on how to improve drug error reporting expressed concern that drugs errors still frequently occur widely despite decades of attempts to address the problem[25]. Armitage noted that 27% of general drug error reports do not identify a contributory factor to the error. He notes regular feedback to staff on drug reports is needed both to improve the rate of drug errors, but also to keep the staff motivated to keep making voluntary reports. The focus of reports must not be on individuals, and individual blame making without justification strongly needs to be avoided, lest voluntary reporting cease. It was noted that assistant persons, like a nurse, were more zealous making drug error reports of *others* than the mistake making doctor themselves. He emphasized that reducing drug errors without getting reporting of drugs errors is very hard, and getting reporting of drug errors therefore has to focus on fixing systems factors and not on individuals.

Focus must also be on human error theory, especially that from aviation. Factors increasing the medication error rate are (i) distractions, (ii) fatigue, (ii) high workloads, (iii) the need to multitask, (iv) and thought process interruptions.

Drug licensing authorities also have a role to play in avoiding approving confusing propriety drug names. Similar sounding drugs lend them selves to drug errors when a verbal instruction precedes drug administration by a second person.

Management must also address the problem of worker burnout. That is currently (2018) an all-time peak professional problem. Thirty two percent of physicians report excessive fatigue, 6.5% report suicidal ideation, and 11% report having made a critical medical error in the preceding three months[26]. Amongst physicians in 2018, anesthesiologists were reported to be the single most burnt-out subgroup of physicians in the USA (Dr. Grant ASA President).

10. HOW TO PREVENT MEDICATION ERRORS AT INDIVIDUAL LEVEL

The remedies are very simple[27].

1. Always **read the ampoule label** before aspirating the contents into a syringe.
    - Regard diluent fluids, like NaCl, as drugs and check their labels as diligently.
    - Reading the box or container label is not the same as reading the ampoule label.
2. Before applying a label to a syringe identify the ampule that was just aspirated to **confirm the same drug name is being applied to the syringe**.
3. Always **read the syringe label** before injecting the syringe.
4. When reading any label **speak the word** or name either aloud, or at the least silently. This means avoid subvocalizing. See the section on subvocalizing. *Don't be shy to speak to yourself- it will save lives.*
5. **Repeat the order**; When administering the drug upon another person's directive always loudly and clearly Say "I am about to inject ……" then pause giving them moment to acknowledge, even if only by their silence, before proceeding. Commonly having two persons working on an anesthetic together more than doubles the drug errors the patient will be exposed to. That results from the added step in many drug administrations of a verbal instruction. The remedy is to verbally verify all drug administrations immediately prior to executing the drug administration.
6. Additional system measures;
    - **Arrange one's drugs** on the anesthesia machine tray and on the drug cart **with a logical system.**
        - Keep the next batch of drugs anticipated to be used close to the front of the anesthesia and to the left, e.g. the three drugs for induction.
        - Keep the non-critical drugs likely to be used in the middle of the tray slightly back from the front, e.g. the next antibiotic dose.
        - Keep the "possibly needed" potent emergency drugs on the anesthesia cart tray to the right and far against the back. This prevents them accidentally being casually used, but still keeps them at hand.
        - Keep all other drugs on the anesthesia supply cart;
            - On the anesthesia cart keep all drugs prepared for the following patient out of immediate reach in and a drawer.
            - Keep all first dilution drugs that need a second dilution for a final syringe in a group pushed to the back.
            - Keep all large volume of surplus drugs, e.g. phenylephrine in a 50 – 100 ml bag
        - Keep both work surfaces as free as possible from clutter with items not essential to the anesthetic.
    - For all high potency drugs (vaso-dilators / vaso-constrictors/ infusion muscle relaxants / remifentanil / propofol infusion); This will prevent dangerous unintended bolus injections at later times.
        - Infuse them into ports as close to the patient as possible. This limits dead space, thus reducing the effect of later unintended drug bolus flushes.
        - Have a routine of clearing the line of all drug with cessation of use of this class of drugs.
        - Use dedicated single channels on a central venous line whenever possible.

- Use color coded syringe tags or labels, for drug classes. It is postulated that this will confine drug errors to within one class of drug. It is believed that a drug swop made within the same class of drug will be less harmful than a drug swop error made across classes of drugs. That is an unproven theory. One complex and questionable study has suggested that total drugs errors were slightly reduced by the use of colored class-specific syringe drug labels. Validation is needed. Counter-argument and anecdote suggest using color coded label *reduces the reading of labels* and may in fact contribute to increased drug errors of multiple syringes are lying around sharing a color class code. Any action that discourages the actual reading of labels has to be avoided primarily. This author will only support color labeling if it is used within strong and highly promoted culture of "read the syringe first".

11. TECHNOLOGY TO PREVENT DRUG ERRORS

This has been reviewed in 2011[28]. This review had many comments. Using **printed drug labels** for syringes eliminates handwriting based errors. Using colored labels is controversial. Whilst drugs can be color grouped e.g. all opiates get blue labels, and all muscle relaxants get red labels, the use of color identification has had little effect reducing medication errors. It is probable that color coding encourages individuals to not read but to rather *recognize* the drug ampule or syringe. Perhaps it narrows the drug errors slightly, to being errors only within a class of drug. One counter argument against color coding is that it forces cognitive reading of all labels, rather than recognition reading.

Colored syringes have also been proposed, but are equally limited in their practicalities and benefits[29]. One reason may be that confusing depolarizing and non-depolarizing muscle relaxants is the single most common error, and both drugs would have the same syringe size and syringe color. Another limitation on color coding is that individual anesthesiologist can have color blindness.

One remedy is to have all **syringes pre-filled** in a pharmacy production line and additionally be bar coded. That would only have conceivable benefit if a syringe could only be injected if it was "approved" after bar code scanning and a prior order had been inserted into medical records. Clearly that is expensive to acquire the extra staff and equipment to manage the system. Also anesthesia is at moments very urgent and the delays in administration of drug and distractions of the technicalities of the processes could endanger patient lives.

Finally, for **bar coding** to work all drugs would have to be administered via one electronic controlled IV access port capable of staying closed if the scanning did not approve the drug.

12. HOW TO MANAGE A DRUG ERROR

If the drug has been injected onto a wrong tissue, instead of IV, two facts become relevant. First the very worst complications can occur. Second protective actions can be applied.

- Wrong drug injected **intrathecal.** Immediately perform a spinal puncture and withdraw 20 ml of CSF. This assumes the patient does not have a non-communicating hydrocephalus. This will remove virtually all of the drug.
- Wrong drug injected **epidural**. Immediately inject 0.9% saline in 5 to 10 ml increments every 5 minutes to accelerate absorption of the drug out of the epidural space.
- Wrong drug onto a **peripheral nerve** in a nerve block. Immediately inject 5 to 30 ml 0.9% saline, repeating this every 20 minutes, to accelerate absorption of the drug away from the nerves.
- Drug injected **intra-arterial**. Immediately aspirate 60 ml of blood out of the arterial line. Then flush the arterial line with 10 ml heparinized saline, repeated every 3 minutes a few times. Only remove the arterial line ideally after consulting a vascular surgeon in case he/she prefers to retain the cannula for angiography.

If the drug was injected intravenous, manage the consequences pharmacologically as is specific for the drug. Maintain oxygenation and cardiac output.

Consider making a confidential drug error report if your institution has a trustworthy confidential reporting system, and a non-blame attitude to such reports.

Consider entering a clinical note about the error if that information is critical to ongoing management of the patient by other physicians / healthcare providers.

ALWAYS act in the best interest of the patient’s health, regardless, while they remain under your care.

No moral system demands of you to sacrifice yourself after the event. All moral systems however demand that you strive to be selfless in caring for your patient to your best ability at all times.

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13. CONCLUSION.

Summary how YOU can prevent drug errors;

1. Believe that drug errors occur very commonly.
2. Be obsessive about avoiding drug errors.
3. Regard Sodium chloride as a drug too – check it too.
4. Read the label;
    - Read the label of the box.
    - Read the label of the ampule.
    - Read the label of the syringe.
5. Mentally verify the route prior to injecting, by talking to oneself. (say e.g. "*Epidural*")
6. Mentally verify the dose, by talking to oneself. (Say e.g. "*50 µg*")
7. Mentally confirm the timing, by talking to oneself. (Say e.g. "*End of case, reversing relaxation*")

CONCLUSION

Anesthesia is a victim of its own success. Compared to the high anesthesia associated mortality of, as recently as 60 years ago, anesthesia has become a hundred-fold safer. Modern anesthesia has also made very large and complex surgeries now possible. This may cause some casualness towards the making of drug administration errors.

Anesthesia remains the most **supercritical medical specialty** of all medical specialties. Insufficient respect is given to this fact by operating room staff and surgeons. Thus, much distraction occurs and that contributes to high drug error rates.

Drug errors can never be eliminated as there are humans involved in many steps of treating an anesthesia patient. We must however strive very aggressively to minimize the chances of drug errors happening.

The Dhawan review concluded with the quote "*To err is human, but in healthcare to err repeatedly is foolish, and perhaps criminal*"[6]. The implication is that we must be highly concerned for making drug errors, and we must adopt strategies to minimize making drug errors.

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