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NEWSLETTER

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What is Your MH IQ ?

by Charles B, Watson, MD, FCCM, and Barbara W. Brandom, MD

Question Your Understanding of MH:

The anesthesia community has the best understanding of Malignant Hyperthermia [MH] because it is a genetically determined illness that is most often recognized during or immediately after anesthesia with the potent inhalational agents and/or administration of succinylcholine. Moreover, a specific antidote for the MH crisis has been available since the late 1970s, dantrolene sodium. Now dantrolene and other necessary elements needed for emergency treatment of an MH episode are immediately available to anesthesia staff at most hospital and outpatient anesthetizing areas where triggering agents are employed. Death during an MH crisis has undoubtedly decreased since the entity was first identified in the middle of the last century because of anesthesia care givers' increased awareness and ability to treat the crisis.

Your MH "IQ" ?

Test yourself with the following statements. Are they true or false?

1. MH is better understood now, after more than 40 years of anesthesia education, research, and clinical experience, so it is no longer lethal.

FALSE— There may be an improvement in our understanding of MH susceptibility and the MH crisis since it was first identified as a fatal perioperative event with high fever.[1] Indeed, one review of MH in New Zealand reported no deaths from MH crisis from a series of more than 120 crises.[2] Unfortunately there are still patients dying of MH every year. MH episodes, individuals with positive MH biopsies, and MH-like events have been reported to the North American MH Registry (NAMHR) since 1988. While data resources in a registry do not provide an accurate event baseline and many events remain unreported, they do provide a profile of events that take place, and there is no evidence to suggest a decrease in MH-related death or complications. The most recent review of MH Registry data shows an increased, rather than decreased, number of deaths reported.[3]

In addition, there has been skepticism that succinylcholine, alone, causes MH crisis in susceptible individuals.[4,5] Older data from the MH registry and newer data from the Canadian MH experience in recent years clearly show that MH crisis can be induced by succinylcholine administration, alone.[4,6-8] Succinylcholine induced muscle contracture of patients and swine shown susceptible to MH by halothane caffeine contracture testing have been demonstrated.[9,10] While the actual magnitude of the risk associated with succinylcholine, alone, is unknown, it is evident that organizations where succinylcholine may be used with or without triggering inhalational agents should have both the MH antidote, dantrolene, and an approach for management of MH crisis.[11]

2. Fever is a late finding in MH crisis. If we take measures to keep patients warm, temperature monitoring is unimportant.

FALSE—Fever was one of the 3 early signs of MH crisis reported in a majority of patients reported to the MH registry in recent reviews. Indeed it was the first sign of MH in approximately one-third and one of the 3 initial signs of MH crisis in approximately two-thirds of patients recently reported from the MH registry. Temperature monitoring is important and review of data from the MH registry showed that survival after MH crisis was related to core temperature monitoring. It is likely that, when temperature is not monitored and rising temperature is missed, recognition of MH crisis is delayed in a significant number of cases.[3,12,13] Also, temperature and other metabolic monitors are important in the immediate postoperative period as well.[14]

3. MH is very rare—there is one causative genetic mutation associated with MH susceptibility.

FALSE—Depending on the population reviewed, MH crisis has been reported with an incidence ranging from 1:8,000 to 1:30,000 anesthetics. Quarterly reviews of calls to the MH Hotline [800-MH-HYPER] made when a caller suspects MH show that around 30% are MH crisis while most represent other acute processes. Early work focused the problems associated with MH crisis on skeletal muscle abnormalities because of the marked increase in muscle tone seen in many MH events.[15] In recent years there has been a dramatic growth in understanding the genetics underlying MH susceptibility. Susceptible individuals have demonstrated one or more mutations in the calcium release channel [Ca2+] RYR1 gene[16] and in genes for 2 other proteins that interact with RYR1.[17,18] Criteria for establishing a causative

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Methylene Blue and the Risk of Serotonin Toxicity

by Adair Locke, MD

Methylene blue is administered intravenously by anesthesia providers for a variety of clinical uses and may be used with increasing frequency as an intraoperative urologic marker dye due to an indefinite nationwide shortage of indigo carmine. It is a potent monoamine oxidase (MAO) inhibitor, and in combination with other serotonergic agents such as selective serotonin reuptake inhibitors (SSRIs), MB can produce serotonin toxicity in the perioperative period.[1,2]

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Malignant Hyperthermia Misconceptions Revealed

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genetic marker are quite rigorous. In the past linkage to MH susceptibility in one or more families, was demonstrated to loci on chromosomes 1, 3, 5, 7, 17 & 19, but the only genes shown to be associated with MH susceptibility are RYR1 on chromosome 19, *CACNA1S* on chromosome 1, and *STAC3* on chromosome 12. Thus, clinical genetic testing of MH risk has moved beyond the Hot Spots in *RYR1* to include ALL of *RYR1* and 2 other genes, *CACNA1S* and *STAC3*.[19,20] Of the >450 MH-associated mutations identified in RYR1, only fewer than 40 have been shown to be functionally causative as reported by the European MH group (www.emhg.org). Interestingly, characterization of the genetics of families with MH susceptibility shows that more individuals in a family carry the genetic marker than have demonstrated MH crisis.[21] This suggests that a larger group of individuals is at risk for development of MH than the number reported to have had a crisis, whatever the actual incidence of MH crisis may be. About one in 2,000 people has a genetic trait that could support the development of an MH crisis when their muscle is stressed. MH is neither very rare nor the result of a simple genetic defect. Genetic testing is valuable, as it is very specific, and can help identify many individuals susceptible to MH. However, the gold standard for diagnosing MH susceptibility remains *in vitro* testing of viable muscle, with the caffeine-halothane contracture test [CHCT], because genetic testing is only 30-50% sensitive at this time.

4. MH crisis is only seen when susceptible individuals are exposed to one of the potent volatile anesthetic agents.

FALSE—MH crisis is most commonly observed during administration of potent inhalational anesthetics after administration of succinylcholine. Halothane, enflurane, isoflurane, desflurane, and sevoflurane have all triggered MH when used alone. MH following exposure to succinylcholine, alone, is more rare but does occur.[7,8] Thus, an office or surgery center that does not administer volatile anesthetics but keeps succinylcholine available for emergency use must be prepared to treat MH. Fatal MH has even occurred without exposure to any anesthetic.[22]

5. MH crisis is an anesthesia-related syndrome and only occurs in the perioperative period.

FALSE—A small number of patients who are MH susceptible have symptoms during day-to-day life. In fact, some patients who are known to be MH

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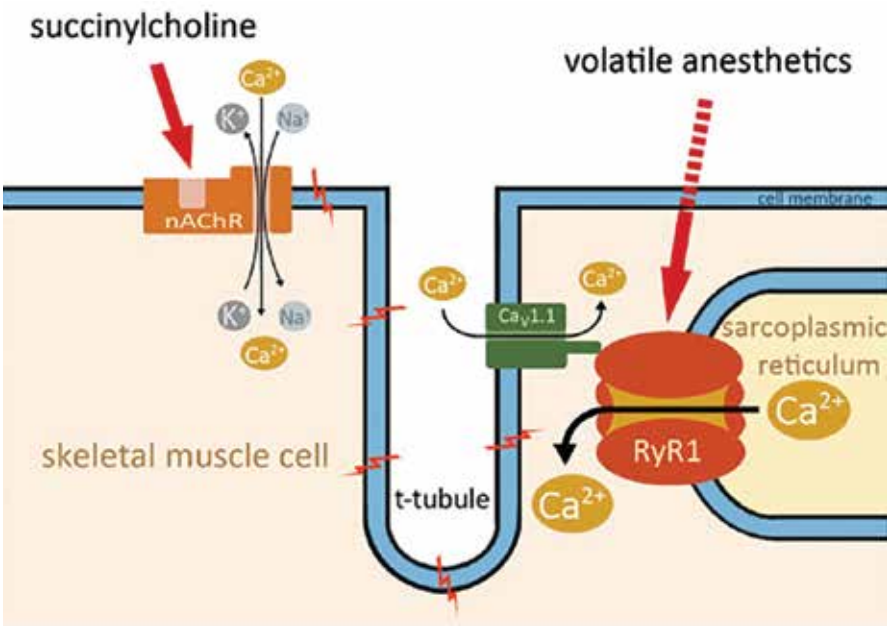

Uncontrolled myoplasmic Ca2+ release is the key to malignant hyperthermia. The most prominent cytosolic Ca2+ elevation results from the freeing of stored sarcoplasmic Ca2+ mediated by ryanodine receptor type 1 (RyR1). While volatile anesthetics stimulate Ca2+ release via RyR1, succinylcholine acts indirectly by activating the nicotinergic acetylcholine receptor (nAChR), a nonspecific cation channel, resulting in continuous local depolarisation. The depolarization can trigger propagated action potentials and will further activate the dihydropyridine receptors (DHPR, CaV1.1) leading to the gating of both Ca2+ release from the SR via RyR1 and L-type Ca2+ current from the extracellular space.

Figure 1. Effects of MH triggers on Ca2+ release. Source: http://www.ojrd.com/content/9/1/8

New Formulation of Dantrolene Much Easier to Prepare

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susceptible have such severe symptoms that they have needed to take oral dantrolene.[23] Recently, it has become apparent that MH susceptibles may experience sudden death under stressful circumstances.[22] This suggests that MH is a stress-related syndrome independent of anesthesia.

6. MH crisis isn't possible if someone has had a number of event free anesthetics.

FALSE—MH has been reported after multiple event-free anesthetics. The largest number of anesthetics reported to the MH Hotline before a patient has experienced an MH crisis is now 20, while Adverse Metabolic or Muscular Reaction to Anesthesia (AMRA) reports in the NAMHR document the median number of anesthetics experienced prior to a MH crisis is 2 and the maximum is 30.[13]

7. It is more difficult to remove "triggering" volatile anesthetics from newer anesthetic machines with high fresh gas flow. Therefore, anesthesia departments should always have a "clean" machine available.

TRUE & FALSE—Some of the newer anesthesia machines may take an hour or more to "wash out" inhaled agents, even when the vaporizers are off, before the machine would be safe to provide anesthesia for an MH susceptible patient. Also, there are commercially available, cylindrical charcoal filters that can be fitted to both ports of a conventional circle system so that agent concentrations are reduced to less than 5 ppm within a few minutes. While these may need to be changed periodically, they can ensure an agent "free," safe machine for the MHS patient who needs anesthesia without triggering agents. Keeping an expensive or outdated "clean machine" in reserve is not necessary.

8. Dantrolene comes in large vials and is difficult to draw up.

TRUE & FALSE—Dantrium® (www.dantrium.com) or Revonto® (www.revonto.com) dissolves in 60 ml of sterile water in under 20 seconds. Dantrolene sodium is not in suspension until it is mixed as it is in a lyophilized powder form. However, the additional time of drawing up 60 ml, injecting it into the vial, and then drawing it up again will take about one minute. Depending on how many personnel are tasked with preparing the full dose of 2.5mg/kg of dantrolene sodium for injection for an average adult, about 10 vials, it may take many minutes to prepare the drug for injection. In addition, 600 ml of fluid will be administered with the full dose.

There is a newer formulation, Ryanodex®, recently available from Eagle Pharmaceuticals that allows a small volume diluent [5 ml] to mix a vial of 250 mg for immediate injection. This formulation can be mixed more rapidly than other lyophilized preparations on the market. Five to ten ml of solution of solution from 2 vials of Ryanodex provides a more than ample loading dose of 2-3 mg/kg dantrolene for large adults. Manufacturer's information can be obtained from http://www.ryanodex.com.

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Indigo Carmine Shortage Leads to Increased Use of Methylene Blue and Its Associated Risks

"Methylene Blue," From Cover

Methylene blue (methylthioninium chloride) is structurally related to tricyclic antidepressants and acts on monoamine oxidase (MAO), especially MAO-A, as well as on the nitric oxide (NO)-cyclic GMP pathway. In addition to its use as a marker dye, it is used in clinical practice for the treatment of hypotensive shock/vasoplegic syndrome, ifosfamide-induced encephalopathy, and methemoglobinemia.[2] Methylene blue has also been used as an infusion to localize parathyroid tissue during parathyroidectomy. In fact, the earliest reports of postoperative neurologic complications associated with the administration of methylene blue were during the perioperative period of elective parathyroidectomies. It is rapidly absorbed in nervous tissue and reaches high concentrations in brain tissue in rat models.[2] Administration of methylene blue in isolation is not thought to confer any significant risk of serotonin toxicity.[3]

Marker dyes such as indigo carmine are commonly used in surgical procedures to confirm ureteral patency and to localize ureteral orifices, for lymph node and vessel delineation, and for tumor localization. Beyond an occasional idiosyncratic drug reaction or mild pressor effect, the intravenous administration of indigo carmine is generally well tolerated. Unfortunately, indigo carmine is not currently available from either of its 2 manufacturers, producing a nationwide shortage. American Regent, Inc., (Shirley, New York) has placed indigo carmine on back order due to manufacturing delays, and Akorn Pharmaceuticals (Lake Forest, IL) has discontinued its production indefinitely due to shortage of raw material.[4] At the author's institution, methylene blue has become the most common choice as an alternative indicator dye. Methylene blue, unlike indigo carmine, is a potent MAO inhibitor and when combined with a variety of medications with serotonergic activity, may contribute to serious sequelae secondary to serotonin toxicity. Specific commonly encountered serotonergic medications include SSRIs like fluoxetine, paroxetine, and escitalopram, serotonin-norepinephrine reuptake inhibitors (SNRIs) like venlafaxine and duloxetine, and tricyclic antidepressants (TCAs) (e.g.,amitriptyline and clomipramine).[5] Even weak serotonin reuptake inhibitors such as intravenous fentanyl, transdermal fentanyl patch, meperidine, tramadol, and methadone have been associated with serotonin toxicity in combination with either methylene blue and / or other serotonergic medications.[7, 8] A more complete list of serotonergic medications can be found on the FDA website.[5] Careful consideration of the concurrent use of these medications in the perioperative period is warranted.

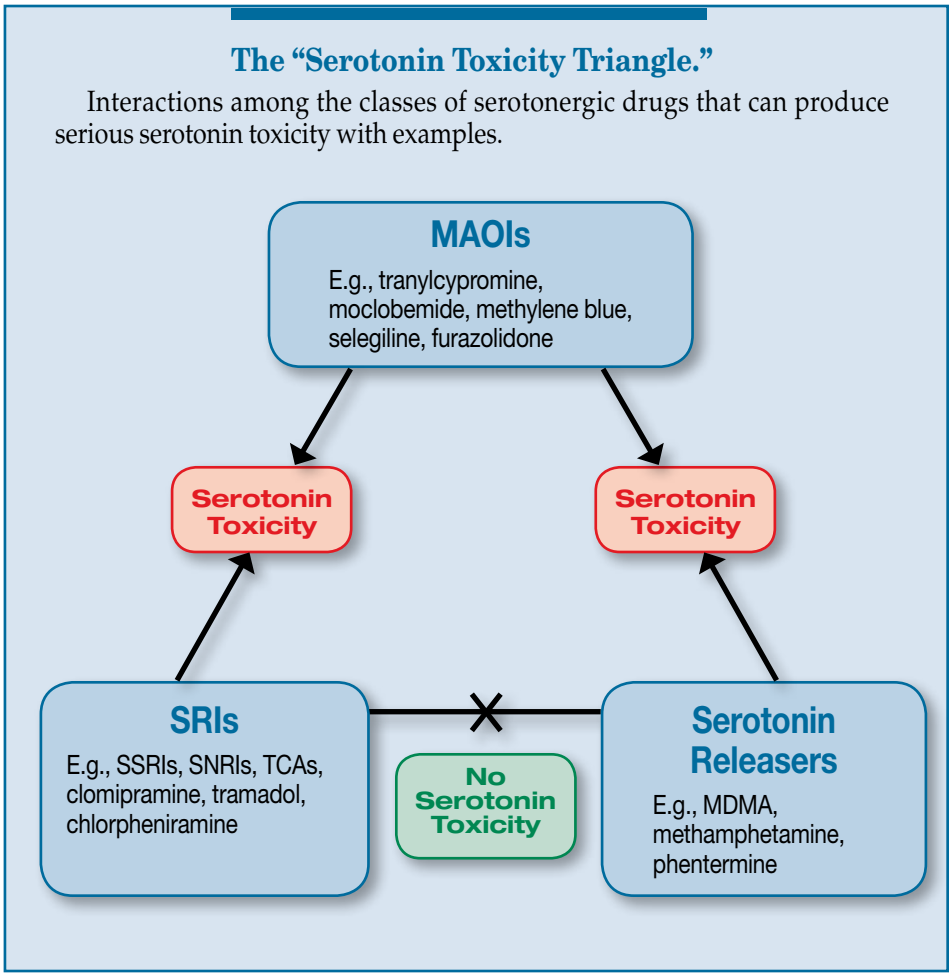

Figure 1. Classes of serotonergic drugs that can produce severe serotonin toxicity with examples (not an exhaustive list). SRI, serotonin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants. Source: Modified from Stanford et al.[5,6,9]

Serotonin toxicity is a result of inappropriately high levels of synaptic serotonin and its severity directly relates to the concentration of serotonin (5-HT) in the synaptic spaces in nervous tissue. Both serotonin releasers like methamphetamine and serotonin reuptake inhibitors (SRIs) have the potential to induce severe serotonin toxicity when administered with MAO inhibitors. Selective and non-selective serotonin reuptake inhibitors increase serotonin by preventing its clearance from the intraneuronal synaptic space. MAO inhibitors prevent intraneuronal metabolism of serotonin, leading to increased release of serotonin from neurons. SRIs by themselves, even if taken in overdose, do not usually precipitate the severe form of serotonin toxicity. However, normal therapeutic SRI doses along with even a single dose of an MAOI like methylene blue may lead to serotonin toxicity as a result of the combination of increased 5-HT release and reduced synaptic 5-HT clearance.[9]

Methylene blue has been used clinically for over a century, but its association with serotonin toxicity has just been elucidated in the last decade. Two surgical case series from 2006 and 2007 describe methylene-blue associated CNS toxicity in patients receiving intraoperative methylene blue. While all patients taking an SRI did not develop CNS toxicity, all of the cases of toxicity involved patients that were taking SRIs. Additionally, there are now at

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Serotonin Toxicity is Potentially Lethal

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least 14 individual published case reports of probable or definite serotonin toxicity involving the concurrent use of serotonin reuptake inhibitors and methylene blue, 1 of which was fatal.[1] A pattern in several early case reports of the serotonin toxidrome occurring with methylene blue administration prompted *in vitro* studies by Gillman and Ramsay in 2006, which were the first to demonstrate MB's highly potent reversible MAO-A inhibitor activity at nanomolar concentrations. Further study has revealed that due to its high potency, even low doses (less than 1 mg/kg) are likely to produce clinically significant MAO inhibition.[2] In July 2011, after receiving reports of serious perioperative adverse events, the FDA issued a safety announcement highlighting the risk of central nervous system dysfunction when administering methylene blue to patients taking serotonergic psychiatric medications.[5]

Because serotonin toxicity represents a spectrum of severity depending on the ability of a drug or combination of drugs to raise serotonin levels, different medications may have more risk of producing serotonin toxicity than others depending on the degree of serotonin augmentation that they produce. Drugs within the same class may have varying effects on serotonin. For example, tricyclic antidepressants (TCAs) cause serotonin reuptake inhibition as well as norepinephrine reuptake inhibition. The degree and selectivity of inhibition of the serotonin versus norepinephrine transport differs among TCAs with clomipramine being most potent at serotonin reuptake while desipramine has little serotonin activity.[10] Other antidepressants such as mirtazapine and trazodone also have low serotonergic activity.[1] Nevertheless, the FDA has extended the warning to all serotonergic drugs and suggests that they be discontinued with anticipated methylene blue dosing until further information is available.

Table 1. Hunter Serotonin Toxicity Criteria

In the presence of a serotonergic agent, serotonin toxicity is established at a high confidence level if any one of the 5 conditions below are present:

1)	Spontaneous clonus
2)	Tremor AND hyperreflexia
3)	Inducible clonus AND agitation OR diaphoresis
4)	Ocular clonus AND agitation OR diaphoresis
5)	Hypertonicity AND temperature > 38° C AND Inducible clonus OR ocular clonus

From Ng et al.[3]

Serotonin toxicity is a potentially lethal condition that manifests with mental status changes, autonomic hyperactivity, and neuromuscular abnormalities. Clinical signs may include tremor, nervousness, agitation, mydriasis, mood dysphoria, hyperreflexia, and inducible clonus. In its most severe form, confusion, muscle rigidity, sustained clonus, and hyperthermia with temperatures greater than 38.5°C may be present. Signs of serotonin toxicity can be mistaken for other conditions in the setting of a recent anesthetic. Benzodiazepines and muscle relaxants may also mask symptoms. Agitation and mood disturbance may be interpreted as postoperative delirium and elevated temperature may raise the suspicion of malignant hyperthermia. Other conditions with overlapping symptoms include anticholinergic crisis, neuroleptic malignant syndrome, acute alcohol withdrawal, and metabolite-mediated opiate toxicity. The combination of a SRI or other serotonergic agent with methylene blue should prompt a high degree of suspicion for serotonin toxicity. The Hunter serotonin toxicity scale is useful to confirm a diagnosis so that immediate treatment may be initiated (Table 1).

Treatment consists of discontinuation of serotonergic drugs, normalizing vital signs with supportive therapy, sedation with benzodiazepines, and cooling therapy for hyperthermia if necessary. Moderate and severe toxicity may benefit from serotonin receptor antagonists such as cyproheptadine, chlorpromazine, or the more potent olanzapine and ketanserin.[2]

Discontinuing a psychiatric medication may not be feasible for some patients, so deciding on an alternative intraoperative marker agent may be warranted, if there are any available for a given surgical procedure. There are reports of indocyanine green being used to identify ureters using near infrared light.[4] Oral phenazopyridine and vitamin B complex may also be considered for preoperative administration. If methylene blue use is being considered, it is advisable to discontinue the SRI to allow clearance of the active ingredient and its active metabolites, with a recommended washout period of approximately 2 weeks for most serotonergic psychiatric drugs. Fluoxetine (Prozac) and its major active metabolite have exceptionally long half-lives and should be discontinued at least 5 weeks prior to the administration of methylene blue. Individual package inserts can provide guidance for discontinuation of these medications in this setting.[11] Many serotonergic medications are extensively metabolized by the liver, so prolonged clearance should be expected in the case of impairment of hepatic metabolism.[12] Methylene blue administration, in the setting of concomitant SRI use, may be considered for life-threatening indications such as vasoplegia with cardiopulmonary bypass, methemoglobinemia, ifosfamide-induced encephalopathy and cyanide poisoning. If the benefit is deemed to outweigh the risk and methylene blue is given, the patient should be monitored for symptoms of CNS toxicity for 24 hours after the last dose of methylene blue.[4]

In summary, the administration of methylene blue in patients taking serotonergic medications, especially SSRIs and SNRIs, may produce serotonin toxicity. With a shortage of indigo carmine, methylene blue may be administered with more frequency especially for urologic procedures. Anesthesia providers should be cognizant of this drug-drug interaction and associated sequelae.

Dr. Locke is an Assistant Professor of Anesthesiology at Wake Forest Baptist Health in Winston Salem, NC.

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AIMS: *Should We AIM Higher?*

by Mark A. Deshur, MD, MBA, and Wilton C. Levine, MD

Adoption of Anesthesia Information Management Systems (AIMS) continues to accelerate. It is estimated that 75% of US academic anesthesiology departments are using an AIMS and that this will rise to 84% by 2020.[1] Within a few short years, it is likely that residents finishing training will have no significant experience charting on paper. AIMS are well poised to become the standard of care for anesthesia documentation.

Adoption has been facilitated by numerous promises, many of which have been discussed in previous *APSF Newsletters*.[2] These include, but are not limited to improved legibility, more accurate data capture, improved chart completion, real-time decision support, more complete charge capture, new opportunities for clinical research, better quality improvement data, and participation in quality outcomes registries.

Multiple studies in the literature support these benefits, though many of these advantages have also been dependent on significant customization or homegrown systems. Customization is necessary because the standard out-of-the-box functionality for many of the popular systems fail to achieve even the most basic of benefits. The literature also suggests the need for substantial financial resources and dedicated staff to support both the implementation and maintenance of an AIMS. As health care dollars become more scarce, this promises to become increasingly challenging. What follows is a review of some of the claims outlined above and a discussion of the current state of AIMS.

Legibility

AIMS have matured anesthesia care documentation from illegible scribble to organized data with clear graphics (Figure 1). It is no longer necessary to decipher another clinician's handwriting when reviewing an anesthetic record or to squeeze comments sideways into the margin to ensure one's thoughts are completely documented.

This advance is not without tradeoffs. A typical 3-hour paper anesthetic record contains 264 data points.[3] In contrast, the same record documented on an AIMS may contain more than 10 times as many data points. Not only do AIMS automatically capture the patient's physiologic and respiratory data with greater fidelity, they frequently require clinicians to manually document substantially more information as well.

Thus, a typical anesthetic no longer fits concisely on a single sheet of paper. It is now necessary to review multiple printed pages or scroll through dozens of screens to view a record in its entirety. These new records are perfectly legible, but often difficult to follow.

Chart completion

There are many studies on chart completion with AIMS. Despite the belief that AIMS automatically improve chart completion, these studies show mixed results. Edwards *et al.* demonstrated a significant improvement in 6 data elements with the implementation of an AIMS.[4] Shear *et al.* reviewed 200 paper records prior to AIMS implementation and 200 records after AIMS implementation. The study evaluated 17 data elements, finding that completion of 7 elements declined and only 1 improved with AIMS implementation. A subsequent evaluation was completed at 7 and 15 months, finding improvement in all deficiencies, yet at levels still inferior to paper charting.[3] This improvement was related to the addition of customized hard stops before record closure, and it emphasizes the opportunity for human factor engineers to further optimize AIMS.

Nevertheless, there is promise. Sandberg *et al.*, looked at allergy documentation in the electronic anesthesia record. At baseline, he found that 30% of charts were missing basic allergy documentation. A customized system was developed to page the anesthesia provider if allergies were not documented within 15 minutes of the anesthesia start time. Following implementation, the missing allergy documentation rate fell to 8%.[5] Similarly, a recent review of AIMS data by McCarty *et al.* demonstrated the ability to improve chart completion. In their study, complete airway documentation improved from 13.2% to 91.6% by using an AIMS in conjunction with deliberate process improvement tools and integrated decision support.[6]

While there is tremendous potential, most chart completion benefits to date have required a homegrown IT solution, locally focused process improvement efforts, and significant financial and clinical resources.

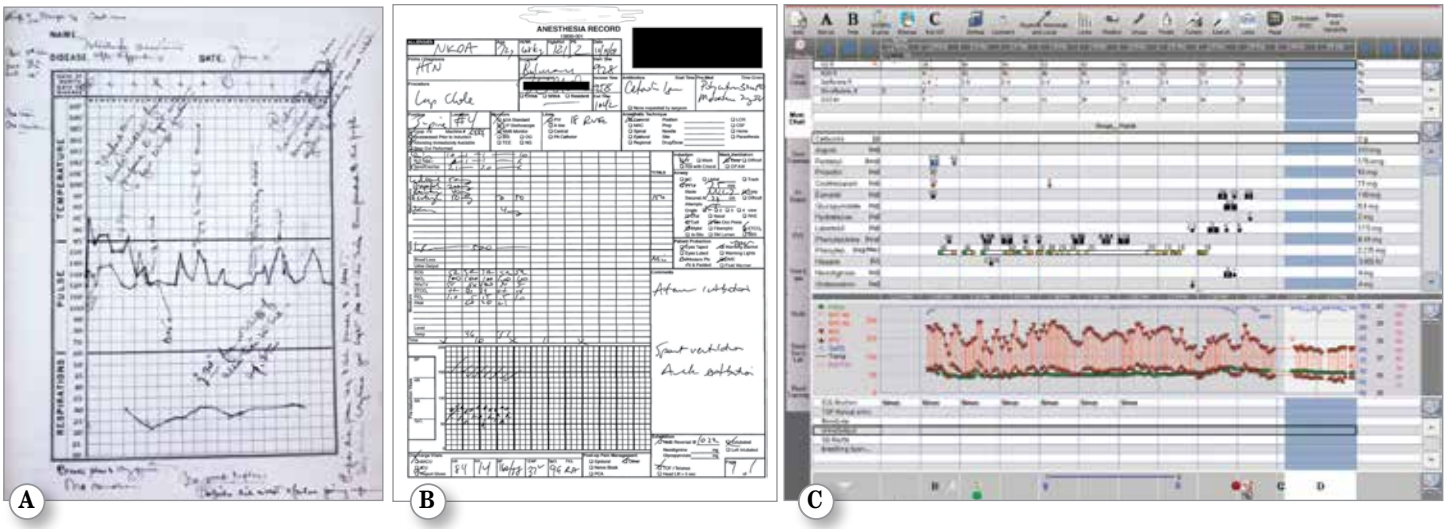

Figure 1:
a) The original Harvey Cushing Ether Chart from 1895 courtesy of Massachusetts General Hospital Archives and Special Collections
b) Modern paper anesthesia record
c) Electronic anesthesia record

See "AIMS," Next Page

AIMS Offers Benefits But Improvements Needed

"AIMS," From Preceding Page

Better Quality Data

AIMS promise to supply us with more accurate and more plentiful quality data. Peterfreund *et al.* developed a secure electronic system to capture quality assurance information linked to an automated anesthesia record.[7] They nearly doubled the number of quality assurance events captured by instituting a hard stop in their AIMS. In addition, the ease of reporting was improved by seamlessly linking the process of quality reporting with case documentation.

In contrast to the improvement shown by Peterfeund *et al.*, the results reported by Pruitt *et al.* at Children's Hospital of Philadelphia show continued cause for concern. They retrospectively reviewed AIMS and Continuous Quality Improvement (CQI) reports of 995 pediatric patients.[8] Observers recorded 8 cases of emesis during induction and all were confirmed with the attending anesthesiologist. However, only 3 were recorded in AIMS records and only 1 was documented in the CQI. While no comparison was made to paper records in this study, it highlights the ongoing challenge to capture manually documented events, even with an AIMS.[6]

Another significant promise is the use of registry data to provide an evidence-based foundation for guiding treatment. By compiling large quantities of data from a diverse group of institutions, it may be possible to identify hidden trends and draw conclusions in new and unique ways. However, it is necessary to remain cognizant of the concept that "garbage in = garbage out." There is often a misguided belief that conclusions drawn from database mining are more accurate. In fact, the quality of this data is poorly understood. In order to truly have comparable quality data, standard data definitions are needed. Groups like the Multicenter Perioperative Outcomes Group (MPOG), the Anesthesia Quality Institute (AQI) and the APSF are currently working to define those terminologies.[9] Until their work is complete, one must read any conclusions with a cautious eye.

Distraction

AIMS have added new complexities to our already chaotic work environments. What used to fit on one side of an 8 ½" x 11" sheet of paper is now buried beneath dozens of screens. Depending on comfort with computers and experience with these systems, there is a very significant potential for distracting a clinician from our primary mission: vigilant patient care.

The distraction risk has been well studied, demonstrating that those who are distracted perform at a level similar to being sleep deprived or intoxicated. One need only observe a car swerving in front of them to realize the dangerous effects of distraction on performance. Indeed, AAA found that as mental workload increases, reaction time slows, brain function is compromised, drivers scan the road less and often miss otherwise obvious visual cues.[10] Though not well studied in the anesthesia literature, it must be assumed that our providers are equally susceptible to these effects.

Discussion

Many of the benefits achieved with AIMS require additional custom programming to bring to fruition. Moving forward, we will need to continue to push the AIMS vendors to incorporate user friendly and meaningful decision support capabilities into their systems.

As you embark on your AIMS journey, we encourage you to follow the path outlined in the literature. You will need a clinical champion who understands your institution's anesthesia workflow and the inner workings of your AIMS functionality. You should seek non-clinical support to help manage, maintain, and troubleshoot any issues as they arise. In many ways, the biomedical team has become equally important as the anesthesia providers in the world of the AIMS.[11,12]

There is no doubt that AIMS are here to stay. They offer a powerful set of tools that promise to improve the care we provide. However, these systems are far from mature and they continue to have significant limitations. We need to be cognizant of their shortcomings, and redouble our efforts to remain vigilant. *After all, next to every AIMS lies someone's loved one.*

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A Statement by the Executive Committee of the APSF

From time to time, the Anesthesia Patient Safety Foundation reconfirms its commitment of working with all who devote their energies to making anesthesia as safe as humanly possible. Thus, the Foundation invites collaboration from all who administer anesthesia, all who supply the tools of anesthesia, and all who provide the settings in which anesthesia is practiced, all individuals and all organizations who, through their work, affect the safety of patients receiving anesthesia. All will find us eager to listen to their suggestions and to work with them toward the common goal of safe anesthesia for all patients.

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- APSF Presents Simulated Informed Consent Scenarios for Patients at Risk for Perioperative Visual Loss Ischemic Optic Neuropathy (18 minutes)

FDA Authority Clarified

To the Editor:

The *APSF Newsletter* in February 2015 carried a piece on drug shortages ("Drug Shortages in the U.S. – A Balanced Perspective"). It seems there may have been an error. The authors indicate that the FDA "has no authority to regulate the quality of manufacturing." The statutory responsibility of the FDA in regulating manufacturing quality goes back many decades. Did the authors mean to write manufacturing quantity?

Sincerely,
Victor C. Baum, M.D.
U.S. FDA
Siler Spring, MD
Email: victor.baum@fda.hhs.gov

Dear Dr. Baum:

We recognize and agree that the FDA has authority to regulate drug manufacturing quality. In our article, we referenced the ISPE's definition of a "quality system" that, in part, is defined as a "system that complies with the regulations enforced by the FDA." In addition, we list factors that may prevent drug shortages such as "Strong Quality Systems that lead to compliance with manufacturing regulations." The FDA indeed has authority to regulate the quality of drugs manufactured and mandate reporting of drug shortages but, to date, has not been granted authority to regulate the quantity and hence the supply of drugs manufactured. We apologize for the typographical error.

Daniel S Orlovich, PharmD

Richard J Kelly, MD, JD, MPH

Improving Post Anesthesia Care Unit (PACU) Handoff by Implementing a Succinct Checklist

by Christopher Potestio, MD; Jay Mottla, GT-2; Emily Kelley, RN; and Kerry DeGroot, MD

INTRODUCTION

Anesthesia providers participate in patient handoffs several times for each patient under their care. Each handoff has the potential for poor communication that may jeopardize patient safety. In fact, a recent study suggested that more operating room (OR) anesthesia handoffs are associated with increased adverse events.[1] With this potential for adverse events in mind, the Joint Commissions 2006 National Patient Safety Goal requires "a standardized approach" for handoffs.[2]

As a quality improvement initiative, our institution has focused on the anesthesia team-to-PACU nurse handoff. The ASA defines the standard for OR-to-PACU handoff: "Upon arrival in the PACU, the patient shall be re-evaluated and a verbal report to the responsible PACU nurse by a member of the anesthesia care team who accompanies the patient." [3] In spite of these guidelines, the quality and quantity of information exchanged can still be variable. Some institutions have adopted standardized handoffs, such as SBAR (situation, background, assessment, recommendation) to try to ensure a quality exchange of information. However, no large scale studies have indicated the best structured approach and no widely accepted guidelines exist for PACU handoff. [4]

Prior efforts to standardize the PACU handoff have been viewed as a burdensome addition to the handoff process. Therefore, our aim was to create a succinct checklist to help expedite the handoff process while increasing meaningful communication between anesthesia provider and PACU nurse.[5] We hypothesized that we would still observe a significant increase in information exchanged despite fewer checklist items. In addition, a more succinct checklist would allow for an easier transition into everyday practice and would avoid the negative response that similar checklists have received in the past.

Figure 1. PACU Handoff Checklist

Patient	Patient Identification (Nameband check)	
	Time In	
	Allergies	
	Surgical Procedure and Reason for Surgery	
	Type of Anesthesia (GA, TIVA, regional)	
	Surgical or anesthetic complications	
	PMH and ASA Scoring	
	Preoperative Cognitive Function	
	Preoperative Activity Level (METs)	
	Limb Restriction	
	Preop Vitals	
Procedure	Positioning of Patient (if other than supine)	
	Intubation conditions (grade of view, airway, quality of bag mask ventilation, bite block?)	
	Lines/catheters (IVs, a-lines, CVSs, foley chest tubes, surgical drains, VP shunt)	
	Fluid Management	Fluids= EBL= UO=
Medications	Analgesia Plan - During Case, Postop Orders	
	Antiemetics Administered	
	Medications due during PACU (antibiotics, etc.)	
	Other Intra-Op Medications (steroids, antihypertensives)	

"Do you have any questions or concerns?"

METHODS

Institutional Review Board approval was obtained prior to this study. To create our checklist, we first used the information published in prior studies and anesthesia textbooks to create an all-inclusive 42 itemized list in a PACU handoff.[5] We modified our checklist to include only data relevant to our institution's PACU handoff process. For example, during casual conversation with our PACU nurses, residents, CRNAs, and attending anesthesiologists, we found that "failed punctures" and "inspection of all lines and catheters" were addressed during a separate nursing assessment so they were excluded from the checklist. This feedback helped reduce our checklist down to 17 items.

The third step of preparing the PACU Handoff Checklist was to measure its effectiveness during actual PACU handoffs. We randomly observed 10 PACU handoffs and screened for additional items exchanged that should be included in our handoff checklist. We found that "preoperative vital signs" and "other medications (antihypertensives and steroids)" were an integral part of the handoffs process but were not included in previous lists.

Our final checklist (Figure 1) included a unique checklist item, "closed loop communication," in order to address two-way communication between PACU nurse and anesthesia provider. Both the ASA and the Joint Commission describe two-way communication as an integral part of any transition of care.

An item was counted as successfully exchanged between anesthesia resident and PACU nurse if the item was mentioned in any capacity. Data collectors were volunteer medical students who were independent from the care team and study team. They observed the handoff without intervention and made no assessment of the quality of the information exchanged. A stopwatch was used to record the time from the start to finish of the sign out. All times were rounded to the nearest second.

We observed PACU handoffs completed by residents of all years of training during the months of April to June, so that all residents had at least 6 months of clinical training before participating in our study. We collected baseline data (Group A) by observing residents complete the PACU handoff without the aid of a checklist. We observed 50 handoffs in this group. The data collectors used the PACU Handoff Data Collection sheet to record the items that were exchanged during handoff as well as the time it took to complete the handoff. The data for these 50 handoffs made up our control group.

See "PACU Checklist," Next Page

Checklists May Reduce Morbidity and Mortality

"PACU Checklist," From Preceding Page

Once baseline data was collected, the checklist was introduced to our residents. Prior to the start of one of our daily academic conferences, each item on the checklist was reviewed with the residents so that they were able to appreciate a successful handoff of information. After this introduction to the checklist, Group B data were collected as residents completed the PACU handoff by using the PACU Handoff Checklist as a guide for exchange of information. The same PACU Handoff Data Collection Sheet was used to record items exchanged and the time it took to complete the handoff.

RESULTS

A total of 14 residents (6 CA-1 residents, 4 CA-2 residents, 4 CA-3 residents) were observed for patient handovers in Group A (control group). A total of 8 residents (4 CA-1s, 3 CA-2s, 1 CA-3s) were observed for patient handoffs in Group B (experimental group). Six residents participated in handoffs in both groups (4 CA-1s, 2 CA-2s). Each resident participated in 1-8 handovers. The percentage of overall items handed off increased significantly with the use of the PACU Checklist (Group B: average, 69.5% +/- 16.5%, Group A: average, 51.50% +/-8.28% p = 0.018) (Figure 2).

Residents who used a checklist (Group B) handed off 8 items on the checklist with a significantly higher frequency compared to residents who did not use a checklist (Group A). These items were: Antibiotics (p = 0.016), Standing Medications (p <0.001), Preoperative Cognitive Function (p < 0.001), Complications (p < 0.001), Patient Positioning (p < 0.001), Limb Restriction (p < 0.001), and Preoperative Activity Level(p < 0.001). They also completed the task of Closed Loop Communication more often (p < 0.001)

While they included significantly more items in their handoff, residents who used the PACU Handoff Checklist spent a significantly longer amount of time completing their handoff compared to those that did not use a checklist (Group B: 126.4 +/- 52.25 seconds; Group A: 100.86 +/- 36.00 seconds, p = 0.011).

The six residents that participated in handoffs in both groups (4 CA-1s, 2 CA-2s) accounted for 28 handoffs in Group A and 20 handoffs in Group B. In a subgroup analysis, percentage of overall items exchanged by this crossover resident subgroup was very similar to the total (Group B [crossover residents]: average, 69.96% +/- 12.62%; Group A [crossover residents]: average 52.23% +/- 8.96%, p = 0.014). They also spent a significantly longer amount of time completing their handoffs with the checklist (Group B: 131.5 +/- 56.43 seconds; Group A: 106.61 +/- 40.44 seconds, p = 0.002).

The more time spent on the handoff, the more items were addressed. Handoffs with the use of the checklist (Group B) spent less time discussing each item than handoffs that did not use the checklist (Group A), although this difference did not approach statistical significance (Group B: 7.71 +/- 3.17 seconds per item, Group A: 8.23 +/- 2.70 seconds per item, p = 0.366).

DISCUSSION

With the use of a checklist, the percentage of items exchanged during PACU handoff increased significantly (Figure 2). The checklist clearly increased the amount of information exchanged during our handoffs; but only 4 out of 50 handoffs included 100% of the information listed. Items most commonly missed include Preoperative Cognitive Function, Lines/catheters, and Antiemetics. Missed items may have been excluded for 2 reasons. The resident may have deemed a particular item non-essential to the transition of care or may have missed the item due to general unfamiliarity with the new tool. In the latter case, further use of the checklist would likely lead to an additional increase in amount of information included in the PACU handoff.

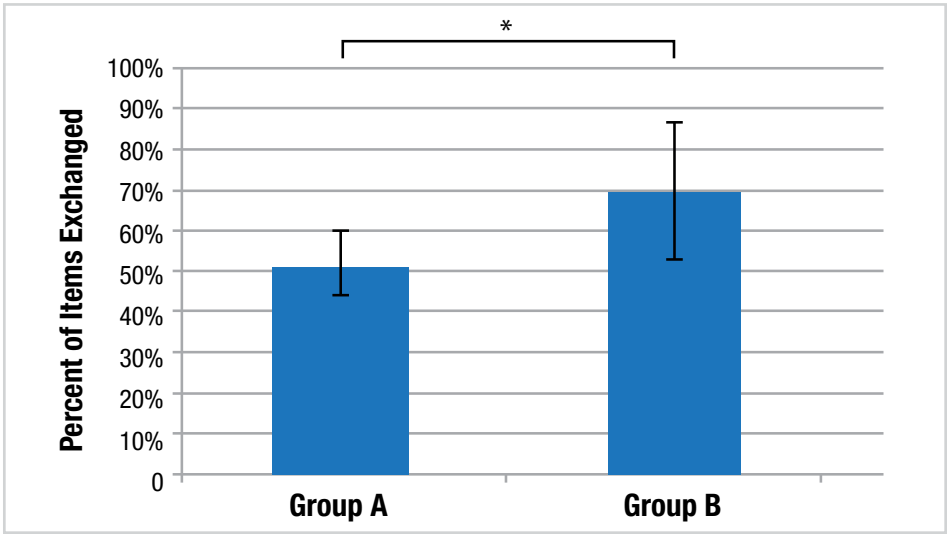

*Figure 2. Percent of items exchanged during PACU handoff. Data were compared using chi squared test. Group B (Checklist) exchanged a significantly higher percentage of important information when compared to Group A (No Checklist). *A significant difference with p = 0.018.*

Failure in communication has been shown to risk patient safety in several studies across different specialties.[6-9] When checklists were introduced to preoperative and intraoperative care, there has been an association with a significant reduction in morbidity and mortality.[10,11] Agarwal and colleagues introduced a standardized handoff tool for transition of care from the operating room to pediatric cardiac ICU. This effort led to a decrease in postoperative complications and an improvement in 24 hour patient outcomes.[12]

In the only randomized clinical trial to date on PACU handoffs, Salzwedel and colleagues surveyed senior anesthesiologists at their institution and constructed a checklist consisting of 37 items integral to their PACU handoff.[5] They found that the use of a checklist for PACU handoff improved exchange of information, but took significantly longer (35 seconds) when compared to handoffs that did not use a checklist. Our study yielded similar results; handoffs in Group B were 26 seconds longer. It appears that the extra time invested in an organized PACU sign out results in more information exchanged. However, the increased burden it places on the anesthesia provider may deter organizations from implementing similar strategies. We quantified this difference by measuring the "velocity" of the handoffs. Group B, with the use of the checklist, exchanged 7.7 items/second which is an improvement over Group A, which exchanged 8.2 items/second without the checklist.

Our study is the first study to target handoffs by residents. At this early juncture in training, an organized PACU handoff may have increased benefit. Without the polished clinical skills and judgment of a seasoned anesthesia provider, residents may be more likely to miss an important piece of information in their sign out.

There were several inherent limitations to our study. Because our data collectors did not record any qualitative data about the information exchanged, we are unable to tell if any errors were made during these handoffs; in fact, we are not able to comment on the quality of handoffs at all, but simply report the percent of items addressed.

Any effort to create a comprehensive sign out tool will invariably increase the length of the sign out while an effort to create an efficient sign out tool will streamline the sign out while possibly excluding vital information. The information that should be included in a complete, thorough PACU

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An Unusual Cause of Hypoxia with Closed Endotracheal Suction System

by Harihar V. Hegde, MD, and Vinayak B. Nayak, MBBS

To the Editor:

Airway suctioning is usually performed by introducing a suction catheter into the endotracheal tube after disconnecting the patient from the ventilator. It can also be accomplished with a closed suctioning system (CSS) included in the ventilator circuit, which allows the introduction of suction catheter into the airway without disconnecting the patient from the ventilator. Closed suctioning technique facilitates continuous mechanical ventilation and oxygenation during the suctioning event. CSS has some advantages compared to the conventional, open-suction technique. It can be helpful in limiting environmental, personnel, and patient contamination and in preventing the loss of lung volume and the alveolar derecruitment associated with standard suctioning in severely hypoxemic patients. The use of closed suction is suggested for adults requiring high FiO_2, or PEEP, or at risk for lung derecruitment, and for neonates.[1]

A patient on mechanical ventilation in our intensive care unit with CSS (Portex® SuctionPro 72™, Dual Lumen Closed ventilation suction catheter with T connector) developed gradual (over a period of half an hour) desaturation while being ventilated in synchronized intermittent mandatory ventilation mode. Common causes for hypoxia in a patient on mechanical ventilation related to endotracheal tube and breathing circuits like kinking, displacement, disconnections, leaks and obstruction, pneumothorax were ruled out by bedside clinical examination. A small quantity of clear aspirate was observed on endotracheal suction. While the cause for desaturation was being actively searched for, we noticed the catheter mount filled with fluid. Upon examination of the CSS it was noticed that the nursing staff had kept connected a 500 ml Normal Saline (NS) bottle to the saline port of CSS (Figure 1) with the intravenous infusion set "on", suction port kept connected to the central suction and thumb control valve in "off" position. NS drops were seen being slowly infused into the breathing circuit. NS was immediately disconnected from the CSS and the catheter mount was drained of fluid. Oxygen saturation improved steadily over the next hour and the patient was subsequently discharged from the ICU after recovery.

In an apparent attempt to reduce the overall time and number of tasks required to perform endotracheal suctioning, the nursing staff had kept the NS connected to the saline port of the CSS. The one-way valve in the saline port is designed to prevent inadvertent saline aerosolization.[2] By attaching the intravenous infusion set firmly to the irrigation port, the one-way valve was in "open" position allowing sustained irrigation of saline leading to flooding of the airway as the infusion set was also kept "on."

Even if it is slightly labor-intensive and time consuming to irrigate saline using a saline filled syringe, saline should not be kept connected to the CSS through an intravenous infusion set. There is no instruction in the product insert regarding how to irrigate or a warning regarding the possibility of inadvertent aerosolization of saline if fluid is kept connected to the irrigation port. This incident is reported to alert the caregivers, especially the intensive care specialists and nursing staff working in intensive care units, about this potential complication associated with CSS.

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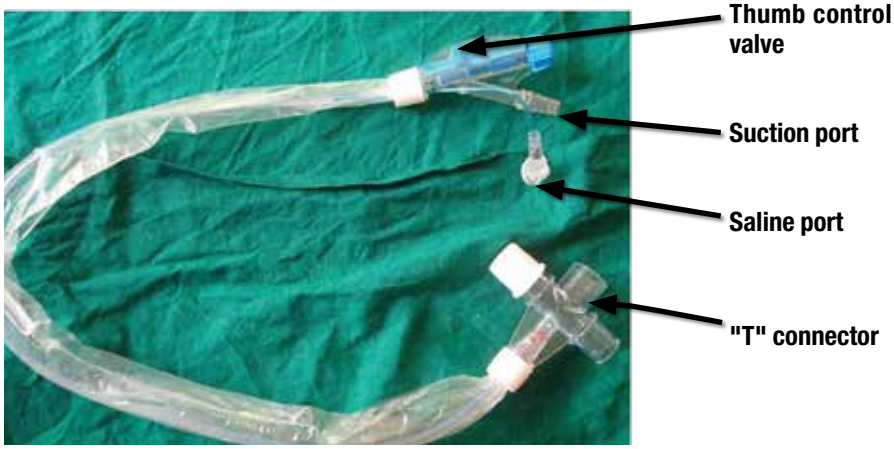

Closed suction catheter that was misused resulting in oxygen desaturation.

Multidisciplinary Process Needed

"PACU Checklist," From Preceding Page

sign out varies greatly from patient to patient; therefore, any standardization tool is often going to be too comprehensive or too efficient.

The anesthesia provider is not the only person providing sign out information to the PACU nurse; our surgical colleagues provide information that is also integral to patient care. Future endeavors will aim to incorporate the surgical handoff in an effort to create a comprehensive, multidisciplinary sign out process. In addition, a larger study will allow us to measure the effect that a standardized sign out process will have on patient outcome.

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