

# Clinical Updates

## Awareness Under Anesthesia (Patient Safety)

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### Introduction

Intraoperative recall and awareness is a rare, but psychologically significant and devastating phenomenon, with an incidence between 0.1-0.2 percent, translating to approximately 20,000-40,000 patients per year<sup>(1,2)</sup>. Discovering methods for detection and avoidance is critical in prevention of long-term consequences, specifically post-traumatic stress disorder.

### Indirect Measures: ERAC and BIS

Intraoperative awareness is defined by explicit (conscious and intentional) memory, along with arousal and experience of surgical events. Current tools used to establish qualitative measurements of consciousness have proven unreliable. Although the brain is the target organ of general anesthesia, direct monitoring of drug effects on the brain does not exist<sup>3</sup>. Therefore, indirect measures like end-tidal anesthetic concentrations (ETAC) and bispectral index (BIS) monitoring currently serve to indicate general levels of consciousness.

ETAC allows for evaluation of minimum alveolar concentrations (MAC), the point at which 50 percent of patients will not move to a surgical stimulus, while BIS monitoring includes spontaneous encephalographic time (burst suppression analysis), along with median and spectral-edge frequency domains to form an index of hypnotic level<sup>3,4</sup>.

Gas analyzers are less useful for anesthetic depth assessment when confounding variables such as hypnotics and opioids are combined with volatile anesthetics. Large scale studies like the B-Aware trial revealed that BIS monitoring reduces the incidence of awareness of at-risk populations by 82 percent when compared to standard patient monitoring with ETAC<sup>5</sup>. However, the follow-up B-Unaware trial refuted the B-Aware results and demonstrated no difference in awareness between BIS and ETAC groups<sup>6</sup>. A recent August 2011 New England Journal of Medicine (NEJM) article concluded no advantage to BIS monitoring over ETAC with respect to intraoperative recall<sup>7</sup>.

Multicenter, prospective, randomized studies like BIS or Anesthesia Gas to Reduce Explicit Recall (BAG-RECALL) analyze high-risk patients<sup>8</sup>. The Michigan Awareness Control Study (MACS) uses specific classes (Class 0: no awareness; Class 1: isolated auditory perceptions; Class 2: Tactile perceptions; Class 3: Pain; Class 4: Paralysis; Class 5: Paralysis and pain; with a "D" designation if distress is included) to categorize levels of awareness<sup>9</sup>. Both large studies were approved in 2009 and are currently in progress to assess the validity of BIS monitoring and ETAC in decreasing awareness and recall.

Subcortical sleep centers, including the pons, midbrain, hypothalamus, and basal forebrain are potential anesthetic targets for awareness prevention. Different anesthetics target different brain regions: propofol induces hypnosis by inhibiting histaminergic transmission from the tuberomamillary nucleus, halothane by reducing cholinergic transmission through the pedunculo-pontine and the laterodorsal tegmentum, and dexmedetomidine by activating  $\alpha_2$ -adrenergic receptors along with inhibition of noradrenergic projections from the locus coeruleus. Subjective experience involves a feedback, or re-entrant neural pathway, with input to the sensory or visual cortex (posterior), followed by impulses traveling "forward" toward the parietal or frontal lobe (anterior), and completed when that impulse returns to the original sensory cortex to form a conscious memory.

Unconsciousness induced by most anesthetics inhibits this anterior-to-posterior "return" feedback activity<sup>10</sup>. At equisedative doses, propofol and midazolam will reliably induce anterograde amnesia, thiopental and similar barbiturates only mild amnesia, and opiates none<sup>11</sup>.

## Demonstrating Awareness

Several methods for demonstrating awareness, in addition to ETAC, have been suggested. The following is a list of potential models that practitioners may use to assess awareness:

1. The PRST score utilizes the parameters of blood pressure, respiratory rate, sweating, and tear production to indicate sympathetic stimulation<sup>12</sup>. These parameters are often extended to include capnography and oxygen saturation, along with reflexive or purposeful movements<sup>13</sup>.
2. Mid-latency auditory evoked potentials (MLAEPs), in which an auditory tone or click is presented to the patient followed by observance of cortical processing via EEG approximately 20-70 msec later, are suppressed with increased anesthetic depth<sup>14</sup>. Those patients with preserved MLAEPs were unable to recall explicit surgical events, but implicit memory (unconscious, non-declarative memory) was preserved, while increased latency suppressed both explicit and implicit recall. The brainstem response is relatively insensitive to anesthetics, but these early cortical responses are reliable indicators of both IV and volatile anesthetic depth<sup>15</sup>. It is FDA approved, but not yet marketed in the USA.
3. Electromyographic and somatosensory evoked potential activity from scalp musculature can suggest somatic response to noxious stimuli, but frequent artifact (i.e. electrocautery) can give inaccurate readings<sup>16,17</sup>.
4. The isolated forearm technique uses a blood pressure cuff inflated to above systolic levels, followed by administration of muscle relaxants. The patient is then asked to consciously move the extremity not yet exposed to relaxant: this may or may not lead to explicit recall of the event. This modality was initially utilized for obstetric procedures, but cases longer than 30 minutes would not permit extended compression without pressure-induced nerve blockade as a consequence<sup>18</sup>.
5. Spontaneous electroencephalographic activity monitors, the most common being BIS, attempt to assess awareness and depth of anesthesia without overt patient movement. Low-frequency, high-amplitude waves typically accompany depressed consciousness, but are not wholly reliable when assessing anesthetic depth. Alternative processed EEG monitors using various algorithms are under development, including entropy, Narcotrend, Patient State Index, and SNAP index, but no evidence suggests their superiority to BIS monitoring. The assumption that a general anesthetic is identical or even similar to a sleep state is inaccurate. The brain transitions from unconsciousness to wakefulness over a narrow drug concentration window; therefore, the quantitative BIS values will vary widely with age, pregnancy, abnormal physiologic processes like sepsis, dementia, seizure activity, along with confounding variables like electrocautery and muscle contraction. Delays from 30 seconds to two minutes in BIS monitor response decreases the likelihood that awareness will be caught and managed appropriately<sup>3</sup>.

## Pre-Operative Assessment

Pre-operative assessment is critical in determining at-risk populations and those most vulnerable to awareness. Major inclusion criteria include planned open-heart surgery, critical aortic stenosis, severe pulmonary hypertension, chronic opiate, benzodiazepine, anticonvulsant, and alcohol use, ASA 4 or 5, end-stage lung disease, history of anesthesia awareness, history of or anticipated difficult intubation, ejection fraction < 40 percent, marginal exercise tolerance, total intravenous anesthesia (TIVA), and acute trauma.

Minor criteria include COPD and heavy smoking history, and notably those on beta-blocker therapy as this tends to mask vital sign changes typically indicating light anesthesia<sup>8</sup>. After obtaining a complete history and performing a thorough physical exam, it is important to identify high-risk patients and inform them of the possibility of awareness.

## Intra-Operative Recommendations

The following are intra-operative suggestions to prevent and detect awareness, many of which are derived from the 2006 ASA Task Force:

1. Careful assessment of anesthetic equipment including pumps and volatile anesthetic delivery systems.
2. Patients with cardiac and pulmonary diseases tend to require less anesthesia secondary to hemodynamic compromise, while patients on chronic narcotics or anticonvulsants manifest increased anesthetic needs.
3. Those requiring smaller dosages of anesthetic (i.e. those with poor cardiac reserve) or trauma patients may be candidates for scopolamine or benzodiazepine therapy based on their anterograde amnesic properties, but concern for side effects like emergence delirium remains<sup>19</sup>. The Task Force is equivocal regarding benzodiazepine and/or scopolamine administration after a patient exhibits conscious behavior.
4. Continuous monitoring for patient movement, reflex activity, and response to commands, especially during spontaneous ventilation, will assist in awareness assessment.
5. Anesthetic concentration should be titrated to a BIS reading between 40 and 60 and ETAC to at least 0.5 and 0.7 MAC.
6. Intraoperative hypotension may be more appropriately managed with preload augmentation and/or vasopressors rather than lowering anesthetic concentration. High anesthetic concentrations (MAC > 1.3) can place a patient with cardiovascular and cerebrovascular compromise at greater risk of hypotension, dysrhythmias, and cerebrovascular accidents.
7. When appropriate, use of potent volatile anesthetics over TIVA may be beneficial, since end-tidal measurements can be obtained in real time.
8. If awareness is suspected, it would be best managed with additional benzodiazepines, opioids, sedative-hypnotics, or intravenous local anesthetics to decrease painful experiences if the patient experiences awareness.
9. Use of paralytics increased incidence of awareness to 0.18 percent from 0.10 percent when they were not used, indicating paralysis with suboptimal sedation and hypnosis.
10. Use careful judgment in determining which patients are at higher risk and may benefit from BIS monitoring. When warranted, brain function monitoring is beneficial in assessing relative, but not definitive, unconscious and awareness states.

## Post-Operative Questions/Protocols

Awareness under anesthesia carries a significant risk of developing post-traumatic stress disorder, with a high proportion exhibiting symptoms after 30 days. If awareness is suspected, the Brice questionnaire has been favored, using five questions:

- 1.) What was the last thing you remembered happening before you went to sleep?
- 2.) What was the first thing you remembered happening on waking?
- 3.) Did you dream or have any other experiences while you were asleep?
- 4.) What was the worst thing about your operation?
- 5.) What was the next worst thing<sup>20</sup>?

Protocols should be instituted, first to apologize and sympathize with the patient as well as offer counseling for any post-operative psychological consequences. A structured interview asking specifics of intraoperative memory should then take place<sup>21</sup>.

## Conclusion

After decades of discussion and analysis, controversy regarding appropriate measurement of anesthetic depth and intraoperative awareness remains. Purposeful movement and appropriate response to commands may still be the best indicators of awareness. Vigilant pre-operative assessment is crucial to awareness prevention. Monitoring may require calibration which is patient-specific. This would necessitate EEG readings prior to anesthetic induction, requiring clinical judgment regarding when a patient becomes unconscious, and correlating such values to that particular patient's awake or unconscious status.

Correlating neural activity with memory continues to elude scientific understanding. Artifacts in these quantitative numbers arise because measurements fluctuate in sensitivity across different anesthetic drugs and types of patients. The most recent analysis reveals that ETAC may be the most useful, although imperfect, method for detecting awareness at this time<sup>3</sup>.

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