Anesthetic Depth, Ventilation and Fluids: Too Much or Too Little

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Department of Anesthesiology
University of Michigan
Disclosures

I have several software patents granted (through the U of Michigan) regarding display technology.

I am the founder, President and have an equity position in AlertWatch, a U of Michigan Startup Company (http://www.alertwatch.com/)
AlertWatch User vs Non-User
6 yrs and 26,769 cases

Process Measures:
- Hypotension < 55 mmHg: <0.001
- Crystalloid ml/kg/hr: <0.001
- Tidal Volume 6-8 ml/Kg Ideal BW: <0.001

Clinical Outcomes:
- MI: 1.5% vs 2.6% vs 2.1% .. Versus no difference
- AKI: .... No difference

Resource Differences:
- LOS: 5 days vs 6 days <0.001
- Hospital Charges: $3,603 less for AW patients
History and Controversies:

Goals: To be knowledgeable of the history, controversies and current thoughts regarding:

1. Anesthetic Depth/Recall
2. Ventilation
3. Fluid Management
Active Alerts

Cumulative time for MAP < 55 = 12 minutes.
Consider documenting train of four.
High cumulative vasopressor bolus dose. Phenylephrine = 500 mcg
H&P has not been signed.

CAUTION: Check monitors and medical record before making medical decisions.
1. Anesthetic Depth

MAC vs Awareness/Recall
Minimum Alveolar Anesthetic Concentration, MAC: A Standard of Anesthetic Potency

Edmond Eger, Lawrence Saidman and Bernard Brandstater
Anesthesiology 1965
After 15 min of Equilibration (Inspired = Expired)

1. Tail Clamp, 30 sec
2. Electrical Stim; 10, 20 & 30 msec “we found 10 to 15 volts very painful when place on our own forearms”
3. Move ETT
4. 20 cm Flank Incision
5. Paw Clamp
After 15 min of Equilibration
(Inspired = Expired)

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   “we found 10 to 15 volts very painful when place on our own forearms”
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They also varied: CO2, O2, BP, Hemorrhage
Ether Day – October 16, 1846
The First Public Demonstration
W.T.G. Morton
Awareness/Recall

First Case was Gilbert Abbott Morton’s First demonstration of Postoperative Recall?

“Feels like my neck’s been scratched”
Incidence? Awareness vs Recall

Isolated Forearm Test (IFT):

- Tunstall ME, BJA 1974: Awareness During C-sec
- Tunstall ME, BJA 1980: Awareness During C-sec

“requested to stay awake” by hand signals to hear her baby, felt no pain.

JD Pandit view: Awareness is a continuum
Russell & Wang: Awareness is all or none, BJA 2015

Up to 30% of Patients will respond to “Move your hand” under a MAC of 1.0 or a BIS of < 60
Brice Questionnaire

1. What was the last thing you remember before going to sleep?
2. The First thing you remember when you wake up.
3. Do you remember anything between?
4. Did you dream?

.. At 24 hrs and 30 days

Brice, Hetherington and Utting
Br J Anesth 1970
Incidence?

Awareness with Recall

Sebel 2004  1:800
Pollard 2007  1:14,560
Incidence?
Awareness with Recall

Sebel 2004  1:800
Pollard 2007  1:14,560
Joint Commission 2004/2008
ASA Practice Advisory 2006
The B-Aware Trial

Randomized “Double Blinded”

BIS vs No BIS

2463 pts: 1,225 BIS vs 1,238 No BIS

Awareness 2 vs 11 P <0.02

(1:600) (1:100)

Number needed to Tx 138 ($2,200/pt)

Myles et al The Lancet 2004
B-Unaware Trial

2,000 High Risk Patients*
Randomized BIS vs ETAG
( >60) (MAC< 0.7)
Brice Interview at 24 hrs and 30 days

Avidan et al NEJM 2008
B-Unaware Trial

2,000 High Risk Patients*
Randomized BIS vs ETAG
(>60) (MAC< 0.7)
Brice Interview at 24 hrs and 30 days

2 patients in each group had Recall

Avidan et al NEJM 2008
B-Unaware Trial

2,000 High Risk Patients*
Randomized BIS vs ETAG
(>60) (MAC< 0.7)
Brice Interview at 24 hrs and 30 days

2 patients in each group had Recall
BIS Didn't Help

Avidan et al NEJM 2008
ASA ... What to Do?

BIS a Standard of Care?
ASA ... What to Do?

BIS a Standard of Care?

ASA/FAER RFP

$1,000,000

Jan 2008

Mike Avidan $500,000; Wash U

George Mashour $500,000; U of M
WHERE TO START?

1. What is our incidence?
   (need to know to determine sample size, Power analysis)

2. How to account for Infusion anesthetics?
   ... Propofol, Dex
WHERE TO START?

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   (need to know to determine sample size, Power analysis)

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3. Need a Scale?
WHERE TO START?

1. What is our incidence?
   (need to know to determine sample size, Power analysis)

2. How to account for Infusion anesthetics?
   ... Propofol, Dex
   Need to develop an new “MAC equation “

3. Need a Scale?
   MACI 1 through 5 with D
Incidence of Self Reported Awareness/Recall

A review of 116,478 post op visits

Most common in MAC and Regional Case?

They expected complete amnesia and we provided it 90% of the time.

After GA = 1/4401


A Novel Electronic Algorithm for Detecting Potentially Insufficient Anesthesia

MAC Aware equation was retrospectively applied to 4 yrs of cases including 12 awareness cases

MAC* < 0.5 (age adjusted) highest likelihood

Mashour et al J Clin Mon & Comp; 2009
MAC Aware

MAC (Minimum Alveolar Concentration) Formula

MAC* =

\[
\text{Propofol rate (in mcg/kg/min)} / 150 + \text{Demedetomidine adjustment} + \frac{\text{Expired Sevoflurane}}{1.8} + \frac{\text{Expired Isoflurane}}{1.17} + \frac{\text{Expired Desflurane}}{6.6} + \frac{\text{Expired Nitrous}}{104} \times 10^{(0.00269 \times (\text{age of patient} - 40))}
\]
A NOVEL CLASSIFICATION INSTRUMENT FOR INTRAOPERATIVE AWARENESS EVENTS: MACI (Michigan Awareness Classification Interment)

Class:

1. Auditory perceptions
2. Tactile perceptions
3. Pain
4. Paralysis
5. Paralysis & Pain

D modifier if associated with Distress

Mashour et al A & A 2010
3 & 4 Years later ...

Avidan & Mashour NEJM 2011
Mashour & Avidan Anesthesiology 2012
A total of 27,314 consented & interviewed patients
3 & 4 Years later ...

Avidan & Mashour NEJM 2011
Mashour & Avidan Anesthesiology 2012

A total of 27,314 consented & interviewed patients

In both High and Normal Risk Patients
Use of BIS did Not reduce the incidence of Awareness with Postop Recall
Incidence of Definite Awareness

Avidan et al; High Risk Pts: NEJM 2011

BIS Alert = 7/2,861 (0.24%)
Agent Alert = 2/2852 (0.07%)

Mashour; General Pts: Anesth 2012

Over All = 19/18,836 (0.1%)
BIS Alert = 0.08%
Agent Alert = 0.12%
No Alert = 0.38%; P < 0.006
### Awareness Events by Class

**Table 2. Incidence of Awareness by Class**

<table>
<thead>
<tr>
<th>Awareness Classification</th>
<th>Class 1D</th>
<th>Class 2D</th>
<th>Class 3D</th>
<th>Class 4D</th>
<th>Class 5D</th>
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<tbody>
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<td>BIS group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Possible</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
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<td>ETAC group</td>
<td></td>
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**Number of patients**
“Exclusion Criteria”

1. All these studies excluded Pure TIVA

2. The equation does not include Ketamine * or Midazolam

* BIS doesn’t work with Ketamine anyway
1. Anesthetic Depth

Conclusions:

1. Incidence about 1:1,000
2. BIS? Unless High Risk/Pure TIVA (no N2O) & Relaxant
3. Some Type of “MAC” Alert Helps
4. Inform Patients receiving MAC Anesthesia/Regional of Recall
What about Triple Low/Double Low?

Triple Low = Low BIS & BP & MAC

Associated with Hospital Stay and Mortality

Sessler et al. Anesth 2013

Not Associated with Mortality

Kertai et al. Anesth 2014
2. Ventilation
Why did we/ I use 10 ml/kg tidal volumes & RR of 10 in the OR?
"A Concept of Atelectasis"

- Declines in PaO$_2$ and compliance reversible with hyperinflation maneuvers

- **PEEP** had not been “invented” yet

Bendixen et al. NEJM 1963;269:991-996
Bendixen et al Conclusions: 1963

1. “PaO2 decrease with time could be reversed by passive hyperinflation”

2. “Continuous use of large tidal volumes or periodic deep breaths are essential in preventing increased variable shunt”

3. “Large tidal volume appears to protect against falls in oxygen tension”
Result …

TV = 10 ml/kg
RR = 10

(whoever saw a RR of 10 on the floor?)

Became a standard for 50 yrs !!!
Easy to multiply 😊
VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

The Acute Respiratory Distress Syndrome Network.
NEJM 2000;342(18):1301-08.
# ARDS Net Trial NEJM 2000

**ICU Patients with Acute Lung Injury/ARDS**

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*Ideal body weight.

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**ARDS Net Trial NEJM 2000**

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**6 ml/kg Ideal Body Weight**

Editor's Note: Louis Dublin, Chief Actuary of the Metropolitan Life Insurance Company in the 1940s, first formulated a set of "ideal weights" for women in the Statistical Bulletin for October 1942, which was followed in June 1943 by a similar set of "ideal weights" for men. Dublin's concept, which has been largely validated by subsequent research, was that weight gain after age 25 was largely due to increases in body fat and, from the actuarial point of view, was

13 to 14 pounds, or more than 10 percent, and

or more. Such increases are neither necessary

or feasible physical activity decreases.

Longevity is probably the best single index of "h

by the Metropolitan Life Insurance Company. h

ing adult ages a moderate degree of overweight w

about age 35, the advantage lay with women

and beyond, the underweights had the best lo

had at every age. Even in young people, the a

degree of overweight has been diminishing, because two important diseases—
tuberculosis and pneumonia—which have largely accounted for the excess mor

tality among young underweights in the past, have been brought under control.

Indeed, the advantage of overweight at the younger ages is so temporary that if the

whole life span is considered, a moderate degree of overweight even at those ages
A Trial of Intraoperative Low-Tidal-Volume Ventilation in Abdominal Surgery

Emmanuel Futier, M.D., Jean-Michel Constantin, M.D., Ph.D., Catherine Paugam-Burtz, M.D., Ph.D., Julien Pascal, M.D.,

- TV 6-8 vs 10 -12
- PEEP 6-8 vs 0
- RM 30 for 30 every 30

Emmanuel Futier, M.D. et al, NEJM Sept 2013
Lung Protective Ventilation Study

A Trial of Intraoperative Low Tidal Volume Ventilation in Abdominal Surgery

400 pts (200+200)

- TV 6-8 vs 10-12
- PEEP 6-8 vs 0
- RM 30 cm for 30 sec every 30 min

Emmanuel Futier, M.D. et al, NEJM Sept 2013
Lung protective ventilation study

Lots of questions/controversy…
To whom does this apply? etc.
Letter's to the Editor

1. Blum et al “Control not standard of care”

2. Lam et al “Micro aspiration caused bad outcomes, PEEP would have prevented…”

3. Mynbaev et al “Open versus laparoscopic not equal in each group… CO2.”

Blah Blah Blah Blah …. 
Trend in median TV by quarter
Bender et al A&A 2017
Low intraoperative tidal volume ventilation with minimal PEEP is associated with increased mortality

M. A. Levin¹, P. J. McCormick¹, H. M. Lin¹,², L. Hosseinian¹ and G. W. Fischer¹,³*
Low intraoperative tidal volume ventilation with minimal PEEP is associated with increased mortality

M. A. Levin¹, P. J. McCormick¹, H. M. Lin¹,², L. Hosseinian¹ and G. W. Fischer¹,³*

- 29,343 patient records reviewed
• 29,343 patient records reviewed
• Use of **low intraoperative TV** with minimal PEEP is associated with an increase risk of 30-day mortality.
Intraoperative Protective Mechanical Ventilation for Prevention of Postoperative Pulmonary Complications

A Comprehensive Review of the Role of Tidal Volume, Positive End-expiratory Pressure, and Lung Recruitment Maneuvers

Andreas Güldner, M.D., Thomas Kiss, M.D., Ary Serpa Neto, M.D., M.Sc., Ph.D., Sabrine N. T. Herrmes, M.D., Jaume Canet, M.D., Ph.D., Peter M. Spieth, M.D., Patricia R. M. Rocco, M.D., Ph.D., Marcus J. Schultz, M.D., Ph.D., Paolo Pelosi, M.D., F.E.R.S., Marcelo Gama de Abreu, M.D., M.Sc., Ph.D., D.E.S.A.
2. Ventilation

Conclusions:

1. 6 to 8 ml/kg IBW
2. PEEP 5 or Greater
3. Recruitment Helpful

Is it TV, PEEP, Recruitment or all three ???

This makes sense... Until further notice
3. Fluid Management
3. Fluid Management

Too Much of a Good Thing

1. Blood Volume
2. I’s and O’s
3. Fluids
4. “Goal Directed” Fluid Therapy
Estimate Blood Volume

Men = 75 ml/kg
Women = 65 ml/kg
Infants = 80 ml/kg
Neonates = 90 ml/kg
Estimate Blood Volume

Men = 75 ml/kg
Women = 65 ml/kg
Infants = 80 ml/kg
Neonates = 90 ml/kg

What about obese patients?
Fat about 60 ml/kg?
BMI Adjustment?
Prediction of blood volume in normal human adults

155 “volunteers” Angola State Prison Farm
(92 men, 63 women)
Ages 17 to 90
Weights 80 to 390 lbs

Radio-tagged RBCs to measure EBV

Nadler et al  Surgery 1962
Prediction of blood volume in normal human adults

To fit the data he used an “IBM electronic digital computer” ... “a Herculean task by any other method”

$$EBV = 0.3669\times H^3 + 0.03219\times W + 0.6041$$

(for men)

Nadler et al. Surgery 1962
I’s & O’s: Old school

IN’s:
Crystalloid/Colloid/Blood (accurate)

OUT’s:
1. Insensible losses (accurate?)
2. Urine Output (accurate)
3. EBL (not even close to accurate)
4. “3rd Space” Losses (does it exist)
4:2:1 Rule

Santorio Santorio (1561-1636)
Blood Transfusion Management

Transfusion Trigger

&

1 to 1 to 1 (Back to Whole Blood)

I’m not going to Cover this
Crystalloid vs Colloid

Crystalloid: Blood 3 to 1
Crystalloid: Colloid 3 to 1?
Summary:

Crystalloid/Colloid Ratio = 1.5
Meta analysis of 45 studies

“3rd Space Losses “

Surgical Trauma/Edema/Evaporation

Low  2 ml/kg/hr
Moderate  4 ml/kg/hr
High  6 ml/kg/hr

Seems like a lot?

Miller’s Anesthesia 2010
“3rd Space Losses”

Where did this come from?
&
Where did it go?
“3rd Space Losses”

Studies in the 1960’s using radio tagged Alb, RBCs note fluid shifts with larger abdominal surgery

Shires et al Ann Surgery 1961
“3rd Space Losses”

Improved Surgical Techniques, less tissue trauma, Laparoscopic Approaches etc

In 42 of 140 cases EBL < ABL*
If ABL < 500 ; EBL OK
If ABL > 500 ; EBL underestimated

* Actual Blood Loss

Ram et al, Chinese J of Traumatology 2014
“Goal Directed” Fluid Therapy

GDT is defined as:

1. Any use of hemodynamic monitoring and therapies during the perioperative period to achieve a predetermined hemodynamic end point

2. Explicit Protocol to achieve end points Using PACs, Fluids, inotropes ...
“Goal Directed” Fluid Therapy

Based on original studies by Shoemaker
“Supranormal DO2” CCM 1988
Used PAC and Colloid Tx

Replaced by noninvasive Stroke Volume techniques

1. Esophageal Doppler:
2. Pulse Contour:
   Thoracic Bioimpedance *
Several Methodologies to Estimate Stroke Volume

LiDCO+plus LiDCO®
(http://www.lidco.com/product/lidcoplus/)

Surgical

Immediate and Reliable Hemodynamic Picture
ccNexfin system provides a hemodynamic overview within two minutes of starting and connects to the patient by simply wrapping an inflatable cuff around the finger. The pulsating finger artery is “clamped” by applying equivalent counter pressure that results in a pressure waveform.

This is how ccNexfin system provides beat-to-beat, continuous blood pressure in a totally noninvasive manner, thus without the need for arterial cannulation. The resulting blood pressure waveform serves as the basis for the measurement of continuous cardiac output.

Noninvasive, Continuous Hemodynamic Monitoring
ccNexfin System
Protocols to “Optimize SV”

1. Induce GA
2. Measure SV
3. Place in Trendelenberg
   If SV increases Tx Hespan
4. Supine, Re-measure/repeat
   until SV does not increase

Meta Analysis of GDT
Mortality Reduced only in High Risk Group:
> 20% Expected Mortality!

Cecconi et al
Critical Care
2013
OPTIMISE Study Group
(European Study, Multicenter)

1. 734 Pts Randomized GDT vs Usual Care GI Surgery
2. Study Group: LiDCOrapid to max SV with Colloid and Dopexamine

Results: No Difference
Conclusion: GDT did not reduce complications or 30 day mortality

Pearse et al JAMA 2014
More Recent Studies

COGUIDE: Stens et al Anaesthesia 2017

Abd Surgery: cc Nexfin Edwards
More Recent Studies

COGUIDE: Stens et al Anaesthesia 2017
Abd Surgery: cc Nexfin Edwards

Results:
No difference in Outcome
Complication Rate:
GDT Group 46.8%
Controls 44.7%
More Recent Studies

Gomez-Izquierdo, et al. *Anesthesiology* 2017

Using an esophageal Doppler (DP12 Probe; Deltex Medical Ltd., UH)

Randomized Control Trial Elective Lap Colorectal: Ileus

218 Pts in ERAS program; **GDT did not improve postop ileus**

---

Fig 2. Algorithm for intraoperative GDT as recommended by Deltex, manufacturer of the Oesophageal Doppler Monitor. The user monitors the response of the cardiac SV to an initial colloid bolus. If fluid responsiveness is present, a further bolus is administered. Where it is absent, the user tracks changes in SV, using a drop of more than 10% as the cue for a fluid challenge.
Great Editorial
D Murry, Anaesthesia 2017

It does work but ...
It does work but ...
we are using the wrong
statistics
It does work but ... we are using the wrong statistics we are unable to prove it
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D Murry, Anaesthesia 2017

It does work but ... we are using the wrong statistics we are unable to prove it only as part of a bundle of care it is not deliverable we need to work on how to deliver it

Or maybe it just doesn’t work
“Avoid Hypotension”

Avoid Fluid Overload
Avoid Awareness
Avoid Vasopressors

What’s left?
“Avoid Hypotension”

Avoid Fluid Overload
Avoid Awareness
Avoid Vasopressors

What’s left?

The Knowns, The Unknowns and the Unknown Unknowns
“Normal Range” for manual determined SPV and electronically determined SPV and PPV

### SPV

![Histogram of SPV](image)

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<th>5th</th>
<th>95th</th>
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<tbody>
<tr>
<td></td>
<td>2.5 mmHg</td>
<td>9.0 mmHg</td>
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<tr>
<td></td>
<td>4.0 mmHg</td>
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*Fig. 2. Per-case median SPV distributions. Distributions determined to be nonparametric; each failed to fit a normal, log-normal, γ, or Weibull distribution. Percentile ranks illustrated across figure headers. SPV = systolic pressure variation.*

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![Histogram of PPV](image)

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*Fig. 3. Per-case median pulse PPV. Distribution determined to be nonparametric; each failed to fit a normal, log-normal, γ, or Weibull distribution. Percentile ranks illustrated across figure headers. PPV = pulse pressure variation.*

Mathis, et al
Anesthesiology, 2017
**“Normal Range” for manual determined SPV and electronically determined SPV and PPV**

**SPV**

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**PPV**

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**SPV (Electronic & Manual)**

**I Love SPV!**
3. Fluid Management

Conclusions:
Aim for “Zero Balance”

1. Short, low EBL Cases: I’s & O’s (no 3rd)
2. Larger, Longer, Higher EBL:
   SPV & Vasopressors (Neo/Vaso/Norepi)?
3. Big Cases Central Monitoring & TEE
The New Goal “Directed Fluid Therapy”

1. Preop euvolemia: Drink Clears up to 2 hr
2. Avoid Bowel Prep
3. Intraop “zero” fluid Balance
4. Objective measure for larger procedures
5. Postop oliguria OK

Gupta and Gan Anaesthesia 2016