Clinical Truths That Are False

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Online Lecture Notes

PDF files of slides

iveccs15.NICUvet.com

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

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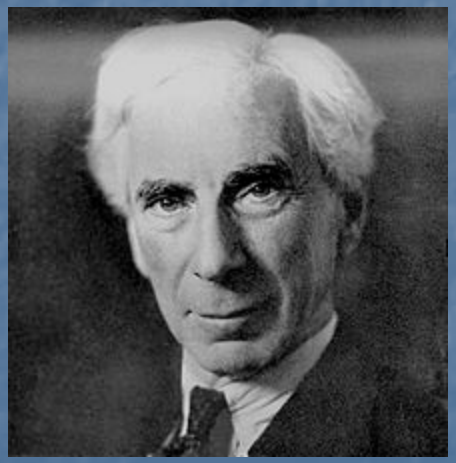
"... it's a healthy thing now and then to hang a question mark on the things you have long taken for granted."



Bertrand Russell

What are Clinical Truths?

- Our long held beliefs
  - How things work
  - Basis of our clinical logic
  - Not often questioned
- Results of clinical studies
  - Easier to embrace new ideas
  - Than to let go of long held “truths”

Making a Case Normal

- Clinical Exam – hoping its normal
  - Physical exam
  - Clinical lab
- Therapeutically manipulations
  - Attempting make the patient normal
- Making a patient “look” normal
  - ≠ make them normal
- Albumin story
  - Historic studies – 25 yr ago
  - Albumin Italian Outcome Sepsis (ALBIOS) study

Clinical Truth: Aggressive Fluid Therapy

- Aggressive fluid therapy
  - Beneficial in hypovolemia secondary to sepsis
- FEAST study - septic children
  - Compensated shock but hypovolemic
  - Treatment with fluid boluses
    - Hypoperfusion
  - Negative outcome

Sepsis
Persistent Inflammation

- Sepsis – inflammation
  - Initial hypermetabolic phase
    - Septic Shock – limited time course
    - Resolution of shock or death
  - If severe inflammation persists
    - With hypoperfusion
    - Multiple Organ Dysfunction Syndrome
    - Represents host defense - new strategy

Multiple Organ Dysfunction Syndrome

- Is adaptive, not pathologic
- Hibernation-like response
  - Sustained severe inflammation
  - Adaptation
    - Decreased energy production – new strategy
    - Normal cellular functioning
      - Stops until inflammation subsides
    - Cells “retreat into their protective shell”
    - “Hibernate” until it is safe
  - New level of homeostasis
    - Maintain the possibility of long-term viability

Multiple Organ Dysfunction Syndrome

- Explanation for ability to recover
  - Lack of tissue necrosis in MODS
  - Ability to fully recover
    - Resume normal function after the crisis is over

Paradigm of Allostasis

- Adaptive phenomenon
  - Body adjusts/adapts stressors
    - Exercise, starvation
    - Sepsis, hypoxia
  - Maintain homeostasis
    - Systems essential for life maintained
- Stress increases allostatic response
- Allostatic overload
  - Sympathetic overload
    - Effect immune, hormonal, metabolic, CV, GI
  - Not able to adjust “allostatic load”
  - Decompensation

Paradigm of Allostasis
Sepsis

- Sepsis – allostatic overload
  - Metabolic demands exceed supply
  - Enter a state of metabolic shutdown
  - As an attempt to restore the energy imbalance
- “Hibernation”
  - Process underlying MODS
- Other stressors compound and reinforce overload
  - Pain
  - Sleep deprivation
  - Constant handling
  - Nutritional stresses

Example: Acute Kidney Injury

- Response of tubular epithelial cells
  - Tissue injury signals “sensed”
    - Distal signals
    - Local signals
      - Renal inflammation
      - Microcirculatory dysfunction
    - Endogenous damage associated signals
      - Release secondary to acute cellular stress
      - Hypoxia, necrosis
  - Adaptive response to threat
    - Protective effect
    - Cell-cycle arrest, hibernation-like effects
      - Until the danger has passed

Example: Acute Kidney Injury

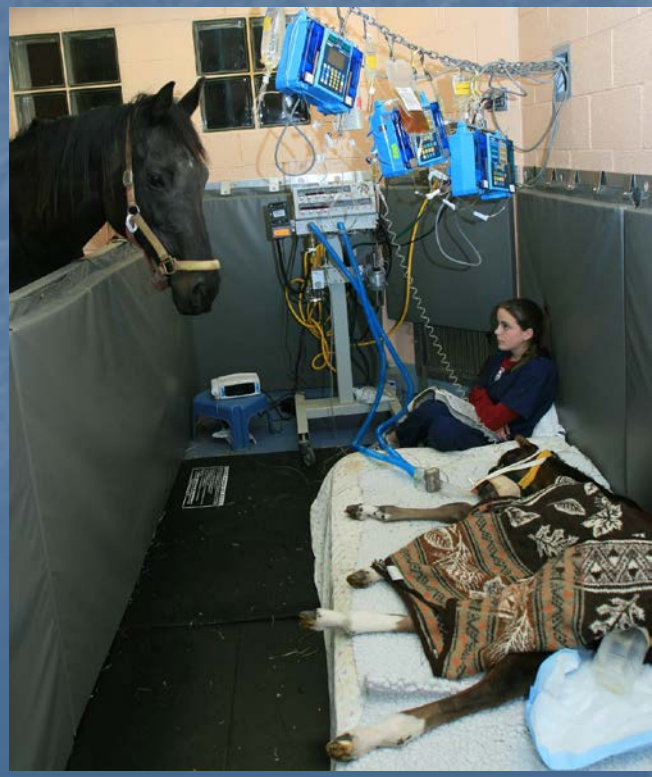
- Remote ischemic preconditioning
  - Cardiac surgery – AKI common
  - Blood pressure cuff on arm
    - Inflate 5 min, deflate 5 min
    - 3 cycles at beginning of cardiac surgery
    - Release “distress” signals
    - Induce protective adaptation
  - Protect against severe AKI
    - Randomized Clinical Trial – JAVMA 2015
    - Also seen in brain, cardiac, other tissues
  - Reprogramming - allostatic overload
    - Genomic, molecular, cellular, tissue levels

Aggressive Fluid Therapy In Sepsis

- Return perfusion
  - After shock but still hypoperfusion
  - Before the inflammatory process subsides
  - Bring cells out of hibernation state
    - Forced to resume normal metabolism
- Negative outcome – FEAST study
  - Work against allostatic overload
- New approach?
  - After septic shock reversed
  - Maintain hypoperfusion – don't correct quickly
  - Control sepsis/inflammation
  - Then treat hypoperfusion

Clinical Truth: Hypercapnic Acidosis Should Be Corrected

- Hypercapnic acidosis is detrimental and should be corrected
- Beneficial effects discovered
  - Permissive hypercapnia
    - Lung protective ventilation strategies
  - Therapeutic hypercapnia
- Hypercapnic acidosis
  - Improves gas exchange
    - Increasing CO_2 removal
    - Improved V/Q matching
    - Improved O_2 unloading (Bohr Effect)
  - Increased respiratory drive
    - Resulting in less apnea



Hypercapnic Acidosis

- Hypercapnic acidosis effects
  - Increase cardiac output
    - Increase in peripheral vascular resistance
  - Reduce endotoxin-induced lung injury
  - Enhance host defense mechanisms
    - Increase proinflammatory cytokines
    - But also anti-inflammatory
    - Immune-modulating capabilities
  - Very complex interactions
  - Aspiration pneumonia
    - Mild hypercapnia
    - Positive effects

Clinical Truth: Hypoxemia is Bad

- Hypoxemia is bad so if in doubt all neonates should be given oxygen

- Hypoxemia – global response
  - Increases blood flow to tissues
  - Ensuring oxygen for metabolism
  - O_2 delivery normal despite hypoxemia
- Example: hypoxemia and encephalopathy
  - Acute, severe hypoxemia
    - Rapid unconsciousness - death
  - Progressive hypoxemia – severe
    - Acclimatization
    - Well tolerated – no disease
  - Need ischemia in addition for disease
    - Hypoxic Ischemic Encephalopathy in neonates

Permissive Hypoxemia

- Permissive hypoxemia
  - Acclimatization
    - Hypoxemia
    - Cellular Hypoxia
  - In subacute/chronic state
- Adaptive mechanisms
  - Allow hypoxia tolerance

“Oxygen Conformance”

- Moderately prolonged hypoxia
- Results in 40 to 60% reduction in O2 use
  - Down-regulation of “non-essential” cellular processes
  - Growth slows/stops
  - Intrauterine Growth Restriction (IUGR)
- Reversible with normoxia
  - No long-term cellular harm
- Chronic adaptive response

Oxygen Conformance

- Preconditioning
  - Better able to survive severe hypoxic event
- Part of allostatic overload response
  - Leading to hibernation-like response
- Facilitates cellular survival
  - Under extreme physiological stress
- Therapeutic Intermittent Hypoxia (TIH)
  - Induced hypoxemia

Is Hypoxemia Bad?

- Birth resuscitation
  - Use O_2?
  - Human infants – room air
    - Asphyxiated neonates lower mortality
    - Spontaneous respiration sooner
- Hyperoxia worse than hypoxemia?
  - Hyperoxemia induces vasoconstriction

Is Hypoxemia Bad?

- Fear of possible hypoxemia
  - Foal may seizure
  - Foal may become unstable
  - O_2 therapy - safety net
- Treating “just in case”
  - Detrimental?
  - Like preloading with fluids

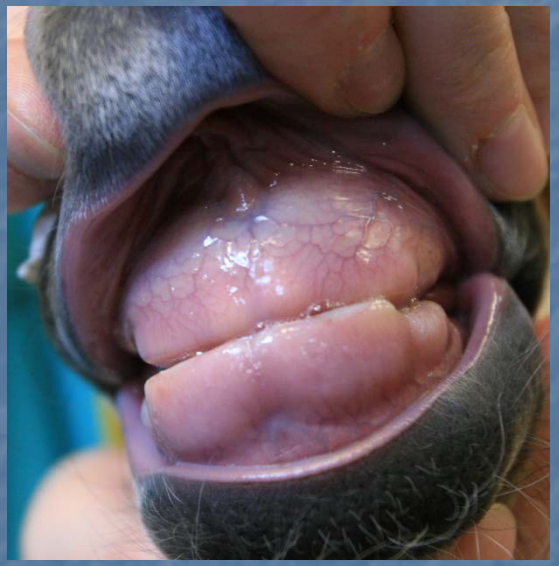
Hypoxemia
When to Treat?

- Oxygen Therapy
  - Significant deficits in delivery
    - Shock
    - Anemia
    - Severe hypoxemia – stress CV, resp systems
- INO_2 in down foals
  - Wait for ABG
  - Changing goals
    - Depends on perfusion, PCV
    - Pao_2 > 60 < 80; SAT > 90%
    - Fear factor

Case Example: Extreme Hypoxemia

- Foal born Saturday night
- Monday
  - Not nursing well
  - Milk drippig from nose
- Endoscopy, Radiographs
  - Venous blood blue
- Bright, normal mentation
  - Good perfusion

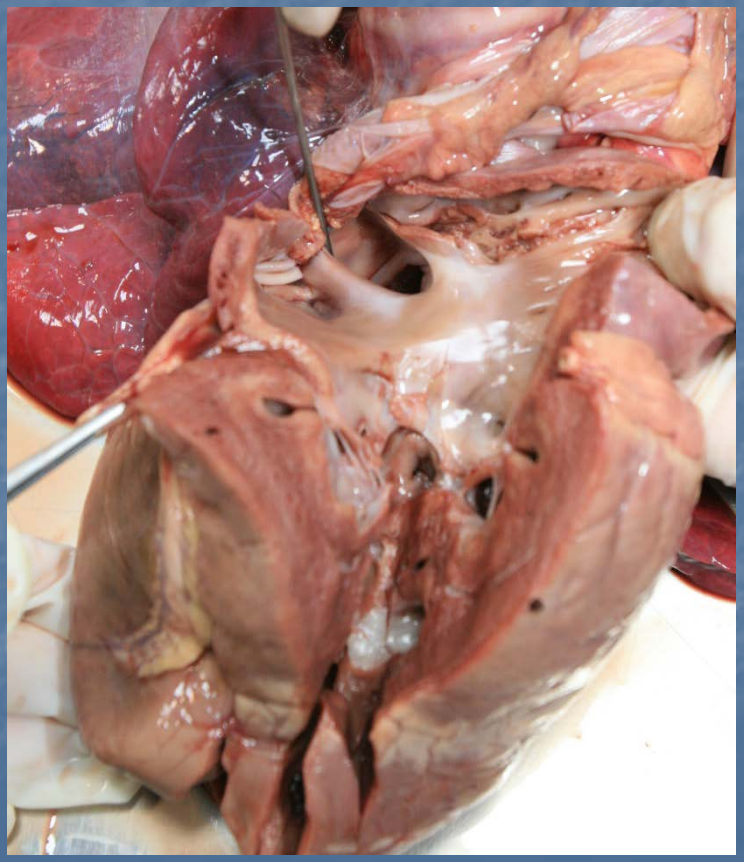
Extreme Hypoxemia Case Example



Extreme Hypoxemia Case Example

	RA	INO_2	Venous
pH	7.369	7.356	7.343
Pco_2	38.3	39.2	44.2
Po_2	21.1	31.6	29.6
BE	-2.2	-2.5	-1.1
SAT	<30	50.4	46.4
Cont	5.7	9.0	7.8

Extreme Hypoxemia Case Example



Clinical truth: Lactatemia is Detrimental

- Lactatemia is detrimental
- Lactate is important metabolic fuel
  - Fetal foal
    - Produced by the placenta
    - Utilized by the fetal foal
  - Neonatal foal
    - Normally present – up to 3 mmol/l
    - Through the first week of life
- Lactate versatile fuel source
  - Produced by all cells
    - Can leave cell
    - Glucose only released by liver, kidney
  - Can be used by any cell

Is Lactatemia Detrimental?

- Septic shock
  - Vital fuel for the heart
  - Important in survival from septic shock
  - Experimental model of sepsis (Lancet)
    - Lactate production blocked
    - Cardiac output not increase with hypotension
    - Infusion LRS
      - Increase cardiac output
- Vital fuel neonatal brain
  - With hypoglycemia – no signs
  - Neonatal foals no measurable blood glucose
    - Don't seizure
    - Don't show expected neurologic signs
  - Preferential fuel for glial cells
    - Over glucose
  - Hypoglycemic neonates
    - Use lactate from protein catabolism
    - Prevent neuroglycopenia

Let go of “Clinical Truths”

Treatments that make “biologic sense”
May not be helpful to our patients.

“Clinical Sense” may not always be enough

to properly care for critically ill patients.

Basis of Practice

Evidence

Traditions

Don’t hold fast to traditions

Beliefs

Be willing to change beliefs

Experience

Known Knowns
Known Unknowns
Unknown Unknowns

...there are known knowns; there are things we know we know...

...there are known unknowns; that is to say we know there are some things we do not know...

But there are also unknown unknowns – the ones we don't know we don't know.

Donald Rumsfeld, US Secretary of Defense 2002

NASA administrator William Graham

British Columbia Royal Commission 1979