Why EBM?
The story from the human medicine side of the fence

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My Purpose:
Cover today:
• What is EBM?
• The 30,000 ft perspective
• Why EBM?
• Why did EBM develop in human medicine?
• How is EBM evolving?

For you to think about:
• Getting to EBVM from EBM and here:
  • The differences between human and veterinary medicine?
  • What can we do about obstacles?
  • Any dangers in this process?
  • Who will (or can) do what?

Looking Across the Fence into the Fog
What can Vet Med learn from EBM’s evolution in Human Medicine?
• Pitfalls?
• Shortcuts?

What is “Evidence-based Medicine”?
EBM is “an approach to practice in which the clinician is aware of the evidence in support of their clinical practice and of the strength of that evidence” (1992, McMaster U, Hamilton, Ontario)

Practicing EBM is simply practicing knowing the answers to two questions:
1. What is the evidence for that?
   • “that” being the use of a diagnostic test, establishing a prognosis, administering a therapy, or recommending a preventive measure
2. How good (strong) is this evidence?
   • How likely are the conclusions based on the evidence correct?

This implies awareness of the kinds of evidence and possession of the skills to critically assess evidence

Most discussions are about how to do this
My purpose is to provide the background on why

Some quick definitions:
Belief:
• State of mind after accepting a concept or idea, becoming part of further related thinking
• Internalized deeply, belief becomes unconscious intuition
• The expert (drives students nuts)

Belief occurs:
• after deliberate, systematic, critical thinking
OR
• with immediate, non-reasoned, uncritical acceptance
• Your choice

• If in error, accepting a more correct belief is more difficult than if no previous belief were held

EBM resulted from the coalescing of Threads:

- Teaching of Literature Evaluation
- Emergence of Clinical Epidemiology
- 1992 term “Evidence-based medicine” first used
- 15 Yrs
- New McMaster PBL Medical Curriculum
- Evolving Computer Technology
- Historical “Tree Shakers”

Note: EBM processes are still evolving!
Learning Cycle

Nature of Human Thinking

"Human nature" is to:
- Weigh information consistent with current belief heavier
- Ignore or discount discordant information
- Typically search for additional belief-confirming data rather than belief-refuting data
  - EX: Selective necropsy to confirm a gross diagnosis (drives pathologists nuts)
- Prior belief biases observation because it subtly changes perception, particularly of vague or ambiguous characteristics
  - EX: Radiographs, clinical signs
- This bias occurs unconsciously and despite the observer’s best intentions!

The fundamental reason for "blinding"!

Evidence-based Belief

Rational Belief:
- A belief that satisfies suitable standards of evidential support

Evidence:
- That which tends to show that something is the case or is used to prove or support something

Implicit in this definition is that evidence varies in strength

The plural of anecdote is not evidence!

Anecdotal Evidence

- The occurrence of desired event(s), such as medical recoveries
  - Case reports
- Often interpreted as due to the therapy applied and thus validating the theory on which the therapy was based
- Problems:
  - The probability of apparently unusual events is considerably higher than expected by intuition (birthday paradox – 30:70%)
  - Unrecognized factors (confounders) may have invalidated the initial prediction
- Because anecdotes are extremely weak evidence, accumulating similar anecdotes does not significantly increase support of a theory – Case series

The plural of anecdote is not evidence!

Analogical Evidence

- Reasoning from comparing known similarities between two systems in which a relationship known to exist in one but not the other is reasoned to exist in the other as well
  - If drug X has been shown to be effective against disease Y in a species Z, reasoning that the same relationship exists between similar drugs, similar diseases or similar species
  - Susceptible to error because of the likelihood that different but unknown factors are operating in the two systems
- Very common reasoning in veterinary medicine
  - Necessary basis for action when empirical evidence is lacking
  - Minor species
- Disease mechanisms are often established in selected species (rodents) and then extrapolated to other species in which direct investigation is impractical

Every little kid is an empiricist: "Don't touch the stove; it's hot!"

Empirical Evidence (Facts)

- Knowledge obtained by looking rather than reasoning or feeling
  - Empirical: based on verifiable observation or experiment, not on theory or pure logic (OED)
  - Objective findings (not their interpretation) derived from formal observational or experimental procedures that are repeatable (verifiable) and that meet currently accepted standards of design, execution, and analysis
- Strengthened by rigorous observation or conducting experiments designed to have a clear, unequivocal supporting or refuting outcome
- Weakened by the degree of opportunity for other explanations that could account for the findings
  - Your judgment as to the impact of this opportunity

The plural of anecdote is not evidence!
Considering Empirical Evidence

- As the opportunity for verification (repeatability) and for assessment of strength is key, the methods used to acquire the evidence must be described or referenced sufficiently to enable this verification and assessment (transparency).

- Remember: The empirical evidence can be correct (e.g., the sun "rises" predictably) but the underlying theory that it is believed to support is wrong (e.g., the sun orbits around the earth).

The importance of the "materials and methods" fine print.

Recognize:

- Most of the veterinary curriculum is taught as dogma (little time to do otherwise).
  - Information necessary to judge its strength is not provided (imagine the length of the notes or textbook).
  - Habits of deliberate, systematic, critical evaluation are not well developed.
  - Uncertainty is hidden (imagine student frustration if it was).
  - Analogical evidence is the basis of reasoning taught in much of the curriculum.
  - Most individual case experience is anecdotal.

EBM Story Timeline & Dignitaries

- Early 1900’s - Ernest Codman’s (1869 – 1940) “The End Result Idea” led to empirical outcome evaluation.

- Florence Nightingale
- Ignaz Semmelweis
- Joseph Lister
- John Snow
- William Harvey
- William Osler

“Tree Shakers” are Important!

Ernest Codman, 1869-1940: A Pioneer of Evidence-Based Medicine: The End Result Idea

- “The End Result Idea: The common sense notion that every hospital should follow every patient it treats, long enough to determine whether or not the treatment has been successful, and then to inquire ‘if not, why not?’ with a view of preventing similar failures in the future.”
- End Result System of Hospital Organization: Tracking and publishing the results of hospitals and of individual surgeons.
- Result: Harvard fired him as surgery instructor.
- Led to establishing the American College of Surgeons.

- acerbic, bitter, flamboyant, eccentric, combative, outspoken
- Codman’s Sign, Classification, Tumor, Exercises, Triangle
- http://www.whonamedit.com/

EBM Story Timeline & Dignitaries

- Early 1900’s - Ernest Codman’s (1869 – 1940) “The End Result Idea” led to empirical outcome evaluation.
- Late 1940’s – Professor Austin Bradford Hill’s (1897 – 1991) use of blinded randomization in a controlled trial of streptomycin for human tuberculosis established the RBCT as the evidence “gold standard.”

RBCT – Randomized Blinded Controlled Trial.

Dogma:

- Those beliefs put forth without supporting empirical evidence with which to judge strength.
  - Not presented for efficiency (textbooks, notes).
  - Unreviewed hypotheses or uncontrolled observation without awareness of the effects of chance, biological variation and observer bias (authoritative or established opinion).
  - Repetition across sources or people, whatever their qualifications, does not change the status of such information (textbooks?).
- Some dogma is right, some dogma is wrong; the problem is which is what?

The importance of the "materials and methods" fine print.

Please Curriculum
Use of randomisation in the Medical Research Council's clinical trial of streptomycin in pulmonary tuberculosis in the 1940s


- Demand for streptomycin, isolated in 1943, far exceeded supply
- Spontaneous cures of the respiratory form occurred, confounding studies
- Prior poorly controlled studies led to the adoption of ineffectual, even harmful treatments
- Blind randomisation relieved the MRC’s clinicians of responsibility for deciding who would be treated
- Trial design was an integration of prior developments rather than novel

AB Hill "quite simply the world’s leading medical statistician"

Physician smoking study with Doll

Established postulates for assessing cause in "The Environment and Disease: Association or Causation?"

*Proc RS Med* 58:295-300 (1965)

http://www.edwardtufte.com/tufte/hill

Even giants stand on giant’s shoulders

**Tables from the original paper**


**Streptomycin cost - $320,000**

<table>
<thead>
<tr>
<th>Radiological improvement</th>
<th>Streptomycin Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate/marked improvement</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Minimal change</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Moderate or slight deterioration</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Marked deterioration</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>15</td>
</tr>
</tbody>
</table>

**Fig 3** Randomization used to make streptomycin and control groups comparable at the outset. Table taken from Bradford Hill’s original paper.

**Fig 4** An independent panel found a clear difference between streptomycin treated and control groups (table taken from Bradford Hill’s original paper).

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**EBM Story Timeline & Dignitaries**

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- Late 1940’s – Professor Austin Bradford Hill’s (1897 – 1991) use of blinded randomization in a controlled trial of streptomycin in human tuberculosis established the RBCT as the evidence “gold standard”
- 1972 – Dr. Archie Cochrane’s (1909 – 1988) bestselling book *Effectiveness and Efficiency: Random reflections on health services*
- Challenged physicians to base the selection of procedures and interventions on the RBCT

**The name behind the Cochrane Collaboration**

http://www.cochrane.org/docs/archieco.htm

Archie Cochrane


- In 1976, Dr. Kerr White, Rockefeller Foundation deputy director for health services, was giving a talk on evidence-based medicine
  
  He was telling his audience that only 15% to 20% of doctors' interventions had been proven to do more good than harm, when a voice yelled out in mid-sentence: "Kerr, you're a damned liar. You know perfectly well that it isn't more than 10 percent!"
  
  The voice belonged to Dr. Archie Cochrane — British epidemiologist, evidence-based medicine pioneer, and a man never afraid to speak his mind

http://www.smj.org.uk/0802/cochrane.htm

**What proportion of Medicine is evidence-based?**

http://www.shef.ac.uk/scharr/ir/percent.html

Resource Guide (Andrew Booth):

- 18 studies, executed between 1995 and 2000, to determine the strength of evidence supporting clinical procedures
- Of ~128 procedures per study (range of 40 to 1,990 procedures)
- 38% were supported by RBCT Type I (strongest) evidence
- 22% were not supported by convincing experimental or non-experimental evidence!

**EBM Story Timeline & Dignitaries**

- Early 1900’s - Ernest Codman’s (1869 – 1940) “The End Result Idea”
- Late 1940’s – Professor Austin Bradford Hill’s (1897 – 1991) establishing the RBCT as the evidence “gold standard”
- 1972 – Dr. Archie Cochrane’s (1909 – 1988) challenging physicians to base the selection of their practices on the RBCT
- Late ’70’s to present – Evidence of problems on a number of fronts began accumulating from studies undertaken after Archie Cochrane’s challenge:
  
  - Problems with current practices
  - Problems with evaluation of new interventions
  - Problems with information dissemination
  - Problems with information synthesis

**Was it really 10%? What is the evidence? Does it matter?**
Evidence of Process Problems

Pseudodoxia pediatrica
NEJM 232:691-697 (1945)

Three groups of pediatricians examined children suffering from tonsillitis:

- 389 11 year old children with tonsillitis
- Examined by physicians

174 (45%) Tonsillectomy Recommend
214 (55%) Tonsillectomy Not Recommend

What do you think the other MD's conclusions were?

Evidence of Process Problems

Clinician-Discoverers – Marshall, Warren, and H. pylori
NEJM 353(23):2421-2423

The Nobel Prize in Medicine 2005
"for their discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease"


Fascinating story of:
- How they challenged the dogmas that:
  - Due to acid, the stomach was sterile
  - Stress and spices cause ulcers
  - Serendipity
  - How advancing technology enable their research
- How the medical community resisted their findings

Challenging Dogma might win you a Nobel Prize

Evidence of Process Problems

NEJM 353(23):2421-2423

Surgeons given written descriptions of surgical problems split down the middle... half recommending surgery, half not

When surveyed again two years later, the same surgeons often disagreed with their previous opinions, with as many as 40% changing their recommendations

In Vermont, the chance of having one's tonsils removed as a child were 8% in one community and 70% in another

Variability occurs because physicians must make decisions about phenomenally complex problems, under very difficult circumstances, with very little support

Physicians are in the impossible position of not knowing outcomes of different actions, but having to act anyway
Evidence of Process Problems

- Cardiologists evaluating high quality angiograms for stenosis of coronary vessels:
  - ... asked to estimate whether the percentage of stenosis ... was greater or less than 50%, they disagreed on 60% of the patients
  - ... on two successive readings of the same angiograms, the observers changed their minds from 8% to 37% of the time, depending on the vessel segment
- In general, observers looking at the same thing will disagree with each other or even with themselves from 10% to 50% of the time
- Pathologists reading human biopsy slides (Not just a clinician's problem)
  A panel of expert pathologists disagreed two or more times on the interpretation of 38% of human skin melanoma biopsy specimens as benign or malignant. (Hum Pathol 27:528-31 (1996))

Are Problems with Current Practices Important?

Evidence of Physician Diagnostic Error Rates
Changes in rates of autopsy-detected diagnostic errors over time:

- 53 autopsy series published 1966 - 2002
- 24% major error rate (4.1% - 49.3%)
- Involved 1st cause of death but did not affect outcome
- 9% class I error rate (0% - 20.7%)
- Likely resulted in death!
- Accounting for steady improvements, current major error rate is likely 8% - 24% and class I rate is likely 4% - 7%

- Of 850,000 individuals dying in US hospitals each year, without misdiagnoses 34,850 would have survived to discharge

Non-randomized comparison results

Table 2. Summary for controlled nonrandomized trials.

<table>
<thead>
<tr>
<th>Preference</th>
<th>Primary</th>
<th>Secondary</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I &gt; S</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>I = S</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>I = S (disap. point/misc)</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>S &gt; I</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>S &gt; &gt; I</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>

“By and large, the distribution leans more favorably toward innovations than that seen in Table 1”

“A tendency for nonrandomized trials to favor innovations is frequently noted”

Science 198:684-689 (1977)

Randomized comparison results

Table 1. Qualitative comparisons between innovations (I) and standards (S) studied by primary and secondary therapies. Where a paper had two comparisons, each was weight ed one-half.

<table>
<thead>
<tr>
<th>Preference</th>
<th>Primary</th>
<th>Secondary</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I &gt; S</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>I &gt; S (successful)</td>
<td>4</td>
<td>49%</td>
<td>8%</td>
</tr>
<tr>
<td>I = S</td>
<td>2½</td>
<td>6</td>
<td>8½</td>
</tr>
<tr>
<td>I = S (different)</td>
<td>1½</td>
<td>19%</td>
<td>5</td>
</tr>
<tr>
<td>I &gt; S (disap. point/misc)</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>S &gt; I</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>S &gt; &gt; I</td>
<td>1</td>
<td>29%</td>
<td>36%</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>28</td>
<td>47* (99)</td>
</tr>
</tbody>
</table>

Science 198:684-689 (1977)

Degree of control vs. Investigator Enthusiasm

Table 3. Degree of control versus degree of investigator enthusiasm for portacaval shunt operation in 53 studies with at least ten patients. The table is revised from Grace, Muench, and Chalmers (B), table 2. a. 682

<table>
<thead>
<tr>
<th>Degree of control</th>
<th>Degree of enthusiasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well controlled</td>
<td>Marked</td>
</tr>
<tr>
<td>Poorly controlled</td>
<td>Moderate</td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Degree of control</th>
<th>Degree of enthusiasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well controlled</td>
<td>0</td>
</tr>
<tr>
<td>Poorly controlled</td>
<td>3</td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
</tr>
</tbody>
</table>

“Muench has a set of statistical laws, one of which says ‘nothing improves the performance of an innovation as much as the lack of controls’”

Because tables for other therapies have similar results, one must be cautious in accepting results of weakly controlled investigations

The rows for "poorly controlled" and "uncontrolled" studies suggest that repeated, weakly controlled trials are likely to agree and build up an illusion of strong evidence because of the large count of favorable studies

Science 198:684-689 (1977)

Gastric freezing for ulcers, ... Human medicine is littered with these!
Do Study Design Weaknesses Matter?

Meta-analysis of empirical studies relating key methodological quality aspects of controlled trials to their effect estimates. Size of squares is proportional to inverse of variance of estimate.

Odds Ratios from trials with inadequate concealment were 30% more "beneficial" than those with adequate concealment.

**You betcha!**

A comparison of results from 182 RCTs with the recommendations of 43 review articles and 100 textbook chapters by publication date.

- Contrast the results from 182 RCTs with the recommendations of 43 review articles and 100 textbook chapters by publication date.
- Classified recommendations of experts as:
  1. Routine – therapy should be used routinely unless there is a specific but uncommon contraindication.
  2. Specific – therapy should be used only in selected patients with a particular indication.
  3. Rare/Never
  4. Experimental
  5. Not mentioned

This study took a huge amount of work! And it had big impact – 606 citations to date.

Not recommending a beneficial therapy

RCT meta-analysis vs. Expert Recommendations

Continuing to recommend a questionable therapy based on biological plausibility

RCT meta-analysis vs. Expert Recommendations

Failure (to date) of the Thorax Pump

Intended to improve blood flow during acute cardiac failure resuscitation.

- (+++) Biological plausibility
- (+++) Lab experimental results
- But equivocal field results to date

Reinforces lesson of the necessity of empirical field evaluation.

Problems with Information Synthesis

The Medical Review Article: State of the Science


  - 34% met 3 of 8 criteria
  - 64% met 4 or 5 criteria
  - 2% met 6 of 8 criteria
  - 6% used quantitative synthesis
  - 42% mentioned future research directives

- These results indicate that current medical reviews do not routinely use scientific methods to identify, assess, and synthesize information
- Medical reviews are often subjective, scientifically unsound and inefficient
- The methods used in this systematic assessment of reviews are proposed to improve the quality of future review articles.

The beginning of converting medical information synthesis into a transparent, replicable and valid scientific process.

Narrative reviews vs. Systematic Reviews
The Medical Review Article Revisited: Has the Science Improved?

Evaluated all the reviews on clinical topics published in 1996:
• 3 of 4 randomly selected core high impact journals (Ann Intern Med, JAMA, NEJM)
• 3 of 8 randomly selected core journals with lower impact factors
• 5 blinded raters used 10 validated criteria

Progress in the wrong direction?

Systematic Reviews: Synthesis of the best evidence for clinical decisions

Systematic reviews assemble, critically appraise, and synthesize the results of primary investigations addressing a specific topic or problem. Systematic reviews are prepared using strategies that limit bias and random error. Systematic reviews are integrative articles. Other examples of integrative articles are economic evaluations, practice guidelines, and clinical decision analyses. Systematic reviews can help practitioners keep up to date with the overwhelming volume of medical literature. Systematic reviews can help ground clinical decisions in research evidence, although they neither make decisions nor obviate the need for sound, compassionate clinical reasoning.

The Science of Information Synthesis

Steps in traditional narrative review
• Write what we think is important
• Find references to support our view
• Insert these as needed

Steps in systematic review
• Question formulation
• Literature search
• Relevance screening
• Quality assessment
• Data extraction and synthesis
• Written report
• Dissemination
• Repeat process to update

Reviews "outsourcing" responsibility for critical evaluation

On-line Systematic Review Systems
The Current Path of Human Medicine

• Developed because:
  ▪ No clinician can read all of the relevant literature
  ▪ Even expert searchers find only half of the RBCTs in MEDLINE
  ▪ Systematic reviews often quickly outdate
  ▪ Busy clinicians do not have the time to practice EBM on a paper-by-paper basis! (Know how to do it? – Yes!)
  ▪ On-line collaborations enable experts at remote sites to cooperate in establishing and updating systematic reviews addressing important clinical questions

Time is the busy clinician’s scarcest resource
Usefulness = (Relevance X Strength) / Work

The Cochrane Collaboration
"The reliable source of evidence in health care"
http://www.cochrane.org/

• International non-profit organisation dedicated to making up-to-date, accurate information readily available worldwide
• Produces and disseminates systematic reviews, promotes the search for sound evidence and develops tools for performing these reviews
• The Cochrane Database of Systematic Reviews is published quarterly http://www.thecochranelibrary.com
• Professionals volunteer to work in a Cochrane Review Group with an editorial team overseeing the preparation and maintenance of the reviews, applying the rigorous Cochrane Review quality standards
• The activities of the Collaboration are directed by an elected Steering Group and are supported by staff in Cochrane Entities (Centres, Review Groups, Methods Groups, Fields/Networks) around the world

Cochrane Reviewers’ Handbook (250+ pages on-line)
http://www.cochrane.dk/cochranehandbook/ithbook.html
Knowledge for Knowledge Translation: The Role of the Cochrane Collaboration

http://www3.interscience.wiley.com/cgi-bin/fulltext/112549281/PDFSTART

- 50 Review Groups
- 10 Methods Groups
- 12 Centres
- 13,000 volunteers

Major undertaking in human medicine

EBM Story Timeline & Dignitaries

- Early 1900's - Ernest Armory Codman's (1869 – 1940) "The End Result Idea" led to empirical outcome evaluation
- Late 1940's – Professor Austin Bradford Hill's (1897 – 1991) use of blinded randomization in a controlled trial of streptomycin in human tuberculosis established the RBCT as the evidence "gold standard"
- Late '70's to present – Evidence of problems began accumulating from studies undertaken after Archie Cochrane's challenge
- 1992 – The paradigm of EBM began coalescing from several pathways to begin addressing these problems
  - Journal clubs, critical review checklists, . . . . > EBM

Graham, ID et al. Lost in Knowledge Translation: Time for a Map?

- There is confusion and misunderstanding about the concepts of knowledge translation, knowledge transfer, knowledge exchange, research utilization, implementation, diffusion, and dissemination
- The implications of knowledge translation for continuing education in the health professions include the need to base continuing education on the best available knowledge, the use of educational and other transfer strategies that are known to be effective, and the value of learning about planned action theories to be better able to understand and influence change in practice settings
- Despite the considerable resources devoted to health sciences research, a consistent finding from the literature is that the transfer of research findings into practice is often a slow and haphazard process

Impediments due to Human Nature

Gordon, ID et al. Lost in Knowledge Translation: Time for a Map?

- A cardiologist coming back from a recent meeting told me that there was a recent trial that showed that the IIb/IIIa inhibitors probably did not reduce adverse outcomes in people who were presenting with acute ischemic syndromes.
- And all the cardiologists got up and said "Wait till the publication's out; we have to look very carefully at that. There may be something wrong with that trial."

By nature, our brains are refractory to new ideas

Gordon Guyatt
(one of the original EBM Gurus)
Resp Care 46(11):1201-1211 (2001)

- So when you're talking about changing behavior, evidence is one relatively small factor in changing anybody's behavior, be it clinicians or other people
- We have to look at other strategies for changing people's minds and, once we've changed their minds, other strategies for changing their behavior
- So there's the rational part of it that we want to get right, and there is also the changing behavior part that we need to get right

Human behavior is hard to change!

Gordon Guyatt
Resp Care 46(11):1201-1211 (2001)

- On the other hand, a recent report of a single big trial suggested that clopidogrel reduces adverse outcome events in people who were presenting with acute ischemic syndromes, given in addition to aspirin
- Everybody walked out saying, "Yes, let's do it."
- People have entrenched biases, beliefs, and ways of doing things. We tend to be resistant to new evidence, and we're more receptive to some new things than others
- If evidence contradicts our general mindset, we're going to be much more resistant

It does little good to change minds if behavior isn't also changed
What Is Evidence-Based Medicine and Why Should It Be Practiced? 
*Respir Care* 46(11):1201-1211 (2001)  
http://www.rcjournal.com/contents/11.01/11.01.1201.asp

- Responding to the limitations of traditional expert recommendations as a guide to clinical practice, evidence-based medicine has presented a paradigm shift in the way clinicians learn and practice medicine
- The practice of evidence-based medicine requires careful examination of the evidence, using a set of formal rules applied in an explicit manner, followed by its judicious application to decision-making, with an understanding of the patient context and values
- We believe that this approach leads to optimal patient care
- At the very least, evidence-based practice facilitates an explicit decision-making process that is transparent and thus open to evaluation and improvement

Society likely will expect this of veterinarians

This is a tough business
*arya J, H Wolford, AH Harken. A Worthwhile Mode of Surgical Inquiry  

- When a physicist drops a brick out the window, it goes down—every time
- When a cell biologist plates out endothelial cells, they grow to confluence—most of the time
- When an aggressive surgical oncologist resects a hepatic metastasis, he or she cures the patient—some of the time
- When a surgical intensivist infuses tumor necrosis factor-binding protein into a critically ill patient, he or she reverses multiple organ failure—almost never

Tough isn’t an excuse clients and society will likely accept

What can we learn from human medicine?
- Where were they when they started?
- How are they getting from there to EBM?
- What problems did the pioneers encounter?
- What problems are they encountering now?
- How are they similar / dissimilar from us?

What should we be learning from human medicine?

Veterinary evidence exists for every human medicine problem I’ve shown you

What we actually said:
- Those who cannot remember the past are condemned to repeat it

From *Reason in Common Sense*, vol. 1 of The Life of Reason

George Santayana  
(poet, philosopher, essayist 1863-1952)

Saying as commonly attributed:
- Those who cannot learn from history are doomed to repeat it

Broader Issues:
Consilience across academic disciplines:
- Do we know & account for our intrinsic mental limitations?
- How do adults (students or practitioners) learn best?
- What motivates or blocks learning? Adoption?
- Basic sciences vs. clinical contexts
- Students dealing with uncertainty
- Clinicians with out-dated paradigms

What knowledge foundation is required:
- To facilitate clinical decision making?
- To facilitate adoption of new paradigms?

Information Science:
- How do we best increase the value of our professional knowledge base?
EBVM is **Personal Protection** in the World of Ideas

**Why “personal protection”?**
Because of the way our minds naturally work if we let them!

- Be very careful what you put in that head, because you will never, ever get it out.  **Cardinal Wolsey** (1475-1530)
- It ain’t so much the things we don’t know that get us into trouble. It’s the things we know that just ain’t so.  **Artemus Ward** (Charles Farrar Browne, 1834-1867)
- It is impossible for anyone to learn that which he thinks he already knows.  **Plutarch**

**As one wag observed, is the only route to change the dying of the “old guard”?**

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**Consider our Learning:**

- Most of the veterinary curriculum is taught as dogma
  - The information necessary to judge its credibility is not provided
  - Lectures, core textbooks
  - Habits of continual deliberate, systematic, critical thinking are not well developed (and, given resource limitations, possibly cannot be)
  - Analogical evidence is the most prevalent basis of reasoning taught in much of the curriculum
  - Most of everyone’s individual case experience remains anecdotal

**Resource Efficiency vs. Educational Efficacy**

**Major Problem: Lack of Quality Evidence**


- **OBJECTIVE:** Evaluate the literature reporting surgical interventions for canine cranial cruciate ligament (CCL) injury using EBVM
- **STUDY DESIGN:** Systematic literature review
- **METHODS:** Search through Medline, PubMed, VIN, and CAB Abstracts performed August 2004 identified 346 sources of information
- **Studies** were evaluated for study design (retrospective, prospective, randomization), surgical technique, short- and long-term follow-up, and evidence classification

**Although we all take science courses and have degrees with “science” in the title, most don’t understand science!**

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**Evidence Classification**

- **Class I:** Systematic reviews based on multiple RCT’s
- **Class II:** High quality clinical trials using historical controls
- **Class III:** Uncontrolled case series
- **Class IV:** Expert opinion or extrapolated from other studies

**This pyramid is important!**

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- **RESULTS:** 28 (12%) sources qualified for evidence classification
- **No class I or class II studies** were present, 5 studies were categorized as a class III and 23 studies were categorized as a class IV
- 17 studies were retrospective and 11 were prospective
- **Proposed results** ranged from a wide variety of subjective findings including clinical impression, radiographic analysis, synovial fluid analysis, gross pathology, and histopathology
- **Objective results,** although infrequent, included force plate analysis and cadaveric biomechanical testing
Evidence Results

- **Class I:** 0 systematic reviews based on multiple RBCTs
- **Class II:** 0 high quality clinical trials using historical controls
- **Class III:** 5 uncontrolled case series
- **Class IV:** 23 expert opinion or extrapolated from other studies

Poor evidence has a price, particularly when its poor quality is not recognized!

Sir William Arbuthnot Lane

**Scottish surgeon, 1856 - 1943**

- Known for developing internal fixation to improve fracture alignment
- Started using silver wire, then screws followed by plates and screws
- Hence, the label "Lane’s plates"


The lack of quality evidence is a consistent finding across EBVM systematic reviews

From some 800+ reports initially identified:

- "We are impressed with the small number of useful reports... while there are hundreds of reports in the literature, most suffer from one or more design flaws or limitations... it suggests that we may be making less than optimal recommendations on vaccine use because of a lack of clinically relevant information."
- "It is time to critically evaluate vaccination as a management tool"

But:

- Eccentric, regarded humans as machines
- Performed many total colectomies as a cure for "auto-intoxication"
- 10% mortality risk

The danger of authorities without supporting evidence

Sir William Arbuthnot Lane

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- During a period in which 60 studies relevant to a particular veterinary clinical question were published in the veterinary literature, 5,400 studies were published in the human literature for the equivalent human clinical question
- Almost a 100 to 1 ratio
- Many of these were based on inherently stronger study designs

Implies that we can not follow the human EBM path exactly

The most significant contribution of veterinary systematic reviews for some time to come will be identifying critical clinical research needs (Also noted by Cockcroft and Holmes)
Dangerous pitfalls for EBVM
Entrenchment and resistance of clinicians

- EBM is arguably the most important contemporary initiative committed to reshaping biomedical reason and practice
- The move to establish scientific research as a fundamental ground of medical decision making has met with an enthusiastic reception within academic medicine, but has also generated considerable controversy
- Cognitive dissonance from the pressure to do something in the face of weak or non-existent evidence?
- EBM and the broader forms of evidence-based decision making has occasioned raise provocative questions about the relation of scientific knowledge to social action across a variety of domains

We are much too small of a profession for EBVM to succeed in the face of clinician resistance

Dangerous pitfalls for EBVM
Not continually making clear the weakness of evidence in each EBM product
- Medical practices, clinical practice guidelines, . . . are claimed to be “evidence based” with increasing frequency
- When is evidence sufficient for “evidence-based” to rightfully apply?
- “Friends” include practitioners of a crude version of EBM (uncritical acceptance of randomized controlled trials while rejecting all other forms of evidence)

Simply labeling something “EBVM” or a “systematic review” does not make it either. Yet it is human nature to do so!

Dangerous pitfalls for EBVM
The myth that veterinary academics alone will create EBVM Simply not enough academic clinician person-hours or $$$

- The number of human oncologists at a typical university cancer center equals all the boarded veterinary oncologists (Keene)
- More physicians have privileges at the University of Washington Hospital than there are veterinarians in the entire state of Washington
- The total 2005 NIH research budget was 28 billion $; the total 2005 USDA research budget was 2 billion $ and ½ of that was for plants

Data ownership issues
- Large entities may recognize a proprietary advantage in their data
- Large livestock units, large corporate practices
- Sources of compensation for data collection?

My proposed solution?
My goal in this paper was to provide entry points for considering EBVM

Make EBVM the Major Mission of the Boards
To generate the evidence-containing literature, I propose that all Boards adopt the requirement of continuing active EBVM evidence generation by all Diplomates
- Diplomates have:
  - self-identified as being interested in a particular clinical specialty
  - the greatest depth of understanding of that particular literature
  - the most to gain from quality evidence
- Everybody has to put their shoulder to the wheel if we are to succeed
- Requires a major paradigm shift in Board mission, structure and function
- Requires changes in many related paradigms, such as the academic reward system for $$$ and papers

Otherwise, I fear that EBVM will remain primarily a “state of mind” for much of clinical medicine

Personal computers and the Internet
The core of the opportunity

- Take full advantage of this technology to facilitate multi-practitioner, multi-center collaboration
- Enables:
  - More rapid case accumulation
  - Broader base for external validity
  - Reduced load per participant

This will not be easy! Or quick! Covey’s “Effective vs. Efficient”

Otherwise, I fear that EBVM will remain primarily a “state of mind” for much of clinical medicine
Emerging Internet Technology

• Internet is evolving rapidly in ways that facilitate community input and discussion
• How can these be used to facilitate EBVM?
• Two examples:
  • Blogs ("web logs")
  • Wikipedia type of software

Evolving Internet Technology

Google "ScienceBlogs"

A community of 40 selected science bloggers, set up as an experiment in scientific communication.

Evolving Internet Communication

Evolving Internet Technology

Google "wikipedia evidence-based medicine"

Enables Community Input & Editing

Primary care practice-based research networks: Working at the interface between research and quality improvement

http://www.annfammed.org/cgi/content/full/3/suppl_1/s12

• PBRNs are clarifying the reasons for disconnects between discovery and implementation, research and practice
• Stakeholders agree on their goals; apply their collective knowledge, skills, and resources to accomplish these goals
• PBRNs appear to be evolving from clinical laboratories into learning communities, proving grounds for generalizable solutions to clinical problems, and engines for improvement of primary care delivery systems

PBRN’s – A useful human medicine model?

A way forward?

1. Establish the structure to manage information translation
2. Assemble species x discipline interest groups and establish the communication structure within
3. Establish criteria for determining the important clinical questions
4. Determine the most important clinical questions
5. Perform systematic reviews on each to establish the state of evidence and identify the weak but critical evidence
6. Establish multi-group collaborative studies to generate strong evidence
7. Update the systematic reviews as evidence becomes available

I don't have all the answers but I believe that for the good of the profession the discussion must start
Our clients do (or soon will) expect nothing less!
Evidence-based Veterinary Medicine: The best discipline intersection for clinical practice