From Bloodletting to Evidence-Based Medicine

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Why consider alternative/complementary/integrative medicine?

- Approached by DVM students
  “Why don’t you teach us homeopathy? You must be close-minded”

- Initially curious, optimistic
  - most modern medicines are derived from natural sources (plants, fungi)
Consider traditional “Western” medicine:
Hippocrates (400 BC Greece) & Galen (2nd century AD Rome)

Adopted ideas of the philosopher Empedocles:
- Universe is made up of 4 elements
  - Earth
  - Wind
  - Fire
  - Water

Applied this notion to medicine
Elements correspond to cold, hot, dry, & moist **humours** in the body

- decided that health results when these are in “balance”

<table>
<thead>
<tr>
<th>Element</th>
<th>Properties</th>
<th>Body Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wind</td>
<td>hot &amp; moist</td>
<td>blood</td>
</tr>
<tr>
<td>Water</td>
<td>cold &amp; moist</td>
<td>phlegm</td>
</tr>
<tr>
<td>Fire</td>
<td>hot &amp; dry</td>
<td>yellow bile</td>
</tr>
<tr>
<td>Earth</td>
<td>cold &amp; dry</td>
<td>black bile</td>
</tr>
</tbody>
</table>

Imbalance → disease
Lacking better technology (microscope, etc.) Hippocrates and Galen knew essentially nothing about physiology or pathology
- could not have conceived rational treatments for most diseases

For example, Hippocrates believed that:

*Sneezing arises from the head, owing to the brain being heated, or the cavity in the head being filled with humours.*


Galen’s writings on human anatomy contain hundreds of errors

Persian physician Al Razi (865-925 AD) recognized many errors in Galen’s views on the treatment of fevers, urinary tract diseases, etc.
Galen’s opinions on the treatment of essentially every disease were applied rigidly in Western medicine for almost 2,000 years.

Historians suspect that Galen would have disapproved (was more progressive)

→ justification for use of bleeding, firing/blistering, etc. to drive out bad humours

e.g. 2\textsuperscript{nd} degree burn $\rightarrow$ infection $\rightarrow$ pus $\rightarrow$ proof that bad humours needed to come out

French physician P.C.A. Louis routinely bled patients suffering from pneumonia.

Decided to assess bloodletting’s efficacy using the new “numerical method” (statistics) to see how many lives he was saving.

Pierre Charles Alexandre Louis, French physician, 1787-1872.
Bloodletting was not considered archaic or harmful: in 1833 France imported 42 million leeches for medical use

According to American physician J.J. Jackson (1836):

*If anything may be regarded as settled in the treatment of diseases, it is that bloodletting is useful in the class of diseases called inflammatory; and especially in inflammations of the thoracic viscera.*


Physicians’ daily application of the therapy, followed by numerous recoveries, provided all the proof they needed that bloodletting was effective
To his dismay, Louis’s statistical analyses showed that bloodletting increased, rather than decreased, mortality.

TABLE 1. Age, number of bleedings, duration of illness, and risk of death according to day of first bleeding in Pierre-Charles-Alexandre Louis’s “Researches on the effects of bloodletting . . . .”

<table>
<thead>
<tr>
<th>Day of first bleeding</th>
<th>No. of subjects</th>
<th>Mean age (years)</th>
<th>No. of bleedings</th>
<th>Duration of disease (days)</th>
<th>Mortality (%)</th>
<th>Relative risk* (95% CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4</td>
<td>41</td>
<td>41</td>
<td>2.8</td>
<td>17.8</td>
<td>44</td>
<td>1.8 (0.9–3.5)</td>
</tr>
<tr>
<td>5–9</td>
<td>36</td>
<td>38</td>
<td>2.3</td>
<td>20.8</td>
<td>25</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>40</td>
<td>2.6</td>
<td>19.2</td>
<td>35</td>
<td>—</td>
</tr>
</tbody>
</table>

Sources: [16, 17].
*Not computed by Louis.
*CI = confidence interval.

FIGURE 4. Survival by day of first bleeding, using data presented in Figures 2 and 3. Bled Days 1–4 (solid line), bled Days 5–9 (dashed line), log rank p = 0.07.
Louis considered his findings

“Startling and apparently absurd…”

but eventually accepted them

Pierre Charles Alexandre Louis, French physician
1787-1872
J.J. Jackson of the Massachusetts General Hospital doubted Louis’s results.

...but found similar results with his own patients when he did a statistical comparison (1825-1834).
“Dr Jackson himself, one of the most careful, and accurate, and sagacious, and matter of fact observers, did not know the results of his experience in the treatment of pneumonitis, till he adopted this system, had counted and analyzed his cases.”

Thousands of years of direct clinical experience with phlebotomy accomplished two things:

(1) It **increased mortality** among patients with systemic diseases such as pneumonia, and

(2) It **convinced millions** of physicians and their patients that it was saving lives.
How did physicians respond to this information?

Not much changed.

Many physicians insisted that clinical experience and tradition were all that mattered, and continued to believe that bloodletting “worked.”

“Bloodletting dominated therapeutics because its success was proven through clinical experience, it satisfied the expectations of patients and physicians, and it was supported by medical theory and tradition.”


Dr Wm Alison
(1790-1855)

- Johns Hopkins U Library
When practitioners claim to have seen any treatment “work” they essentially always mean the same thing:

“I administered a treatment, sometime after which the patient recovered, therefore my treatment caused the recovery.”

This line of thinking completely ignores the role of natural healing.

How do we know that the patient’s body did not heal itself?
Until recently all medicine was based on similar personal experiences

Personal experience can make both effective **AND** ineffective therapies appear to work, so how can we tell which are truly beneficial?
Not from experiences with individual patients, even millions of them

Individual variation is so great that we can only see changes due to therapy by looking at groups

(How long does a cold last? I cannot know how long/severe my next cold will be, only the average behaviour of colds in people)
Clinical success rate

No treatment (Disease runs its natural course)

Treated

Difference attributable to therapy
Over time we have realized that we cannot control our own biases/wishful thinking

- Has led to the randomized, blinded clinical trial
- Done well, can provide accurate knowledge of therapies
- Can be done improperly → misleading results
  - IT IS POSSIBLE TO PERFORM A RANDOMIZED CONTROLLED TRIAL THAT GIVES ERRONEOUS RESULTS
- Must base conclusions on best scientific evidence, not any scientific evidence
  - CANNOT PICK AND CHOOSE FROM AVAILABLE EVIDENCE
- Difficult, expensive to conduct a study that provides accurate information
- A “necessary evil” because we cannot simply “decide” to be unbiased
The scientific method is **not** a cultural tradition, it is a method of examining traditions/beliefs to distinguish between those that are true and those that are false

- Fundamentally **simple** (compare two things → difference?)
- **Democratic**: no-one is “revered”; anyone can make observations to verify or discredit claims
- **Observations** of **nature** drive theory, not the other way around
- **Humble**: continually strives to find & correct errors; acknowledges that not everything is known
- **Universal**: is the study of nature; strives to eliminate cultural biases (e.g. showed that essentially all “Western” medicine based on theory of humours – cupping, purging, bleeding, firing, etc. – was ineffective)
Evidence-based medicine:
“The judicious use of the best available evidence in making decisions about the care of individual patients”
Finding the best information to answer practical questions

- Trisha Greenhalgh, How to Read A Paper: The basics of evidence-based medicine, BMJ 2006

“Evidence-based medicine will provide the most appropriate, substantive, and truly scientific approach to medical decision making.”

- Brenda Bonnett, Chapter 2: Evidence-Based Medicine – Critical Evaluation of New and Existing Therapies
# Evidence-based medicine

**CONSORT 2010 checklist of information to include when reporting a randomised trial**

<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>Item No</th>
<th>Checklist item</th>
<th>Reported on page No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title and abstract</td>
<td>1a</td>
<td>Identification as a randomised trial in the title</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)</td>
<td></td>
</tr>
<tr>
<td>Introduction</td>
<td>2a</td>
<td>Scientific background and explanation of rationale</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>Specific objectives or hypotheses</td>
<td></td>
</tr>
<tr>
<td>Methods</td>
<td>3a</td>
<td>Description of trial design (such as parallel, factorial) including allocation ratio</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3b</td>
<td>Important changes to methods after trial commencement (such as eligibility criteria), with reasons</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>4a</td>
<td>Eligibility criteria for participants</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4b</td>
<td>Settings and locations where the data were collected</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>5</td>
<td>The interventions for each group with sufficient details to allow replication, including how and when they were actually administered</td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>6a</td>
<td>Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6b</td>
<td>Any changes to trial outcomes after the trial commenced, with reasons</td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
<td>7a</td>
<td>How sample size was determined</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7b</td>
<td>When applicable, explanation of any interim analyses and stopping guidelines</td>
<td></td>
</tr>
<tr>
<td>Randomisation:</td>
<td>8a</td>
<td>Method used to generate the random allocation sequence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8b</td>
<td>Type of randomisation; details of any restriction (such as blocking and block size)</td>
<td></td>
</tr>
<tr>
<td>Allocation</td>
<td>9</td>
<td>Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned</td>
<td></td>
</tr>
<tr>
<td>concealment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mechanism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implementation</td>
<td>10</td>
<td>Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions</td>
<td></td>
</tr>
<tr>
<td>Blinding</td>
<td>11a</td>
<td>If done, who was blinded after assignment to interventions (for example, participants, care providers, those</td>
<td></td>
</tr>
</tbody>
</table>
Evidence-based medicine is often misrepresented and then ignored.

“There seems to be a prevailing notion that a doctor can be either evidence-based or compassionate – but not both.”

“EBM is not about ignoring patients and focusing on numbers. I can't imagine how one could be more compassionate than to recommend a therapy that has been shown to be effective, or to be able to give some sort of reasonable likelihood that a therapy will be effective. That seems much more caring than sticking with an opinion that might be wrong.”

- comments from members of EBVMA
We need a serious scientific assessment of traditional claims/beliefs

“We must move beyond a dependence on anecdote, personal experience, and expert opinion.

We must have adequate evidence that our interventions do more good than harm… preferably from randomized controlled trials.

An appropriate comparison group must be in place.”

-Brenda Bonnett, Chapter 2: Evidence-Based Medicine – Critical Evaluation of New and Existing Therapies
Widespread problem:

Personal experience is all that really matters, scientific support is not essential / does not apply / science is misleading

It is exciting to note the thoughtfulness and care that permeates these discussions. As a veterinarian now practising homeopathy and chiropractic almost exclusively, I have all the proof I need every day in my practice to justify these modalities. However, this was not always so. As I entered into the formal study of each of these modalities, I carried with me a big dose of skepticism. Through the process of learning more about the philosophy and theory of these modalities, together with sharing clinical experiences with my chiropractic and homeopathic colleagues, this skepticism was steadily replaced by certainty that these are powerful healing sciences.

As we continue to evolve as a profession, let us at least respect the efforts that each of us put into our careers and

If integrative medicine is to be taken seriously…

“No science, **no knowledge is necessary**, and they who obtain the greatest benefit from this God-sent gift will be those who keep it pure as it is; free from science, free from theories, for **everything in Nature is simple**.”

What if we don’t even try?

If integrative medicine is to be taken seriously…

Clinical success rate

0% 100%

No treatment Treated

Differences attributable to therapy
If integrative medicine is to be taken seriously…

What if we don’t even try?

"It worked for me!"

Clinical success rate

0%

100%

Treated
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Lead talk at Equine Guelph’s first *Integrative Therapies Night*, May 19, 2011