

## HEROES AND MARTYRS OF QUALITY AND SAFETY

# Pierre Charles Alexandre Louis: Master of the spirit of mathematical clinical science

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**P**ierre Charles Alexandre Louis (1787–1872) represented one side in a three way argument about the source of medical knowledge and reasoning which continues today.

Knowledge can come from the physician's long astute clinical experience. This approach goes back to the ancient Greek school of medical empirics 280 BC. The "tripod of the empirics" was to learn from one's own chance observations, to learn from your colleagues present and past, and to reason by analogy ("this patient looks like one I saw before").<sup>1</sup>

In the Paris of Louis's day the second approach to medical knowledge—experimental physiology—was being developed by Xavier Bichat, Claude Bernard, Francois Magendie, and others. They used theory and hypothesis testing on controlled animal experiments<sup>2 3</sup> to show the cause of disease. Today this kind of reasoning might go as follows. Variation in DNA at this location causes these proteins to malfunction causing changes at the cell level which modify organ systems leading to symptoms and disease. This is a logical causal sequence, built on theory, and tested by controlled laboratory experimentation.

Louis brought a third approach—his mathematical method. He carefully recorded for many patients their characteristics, symptoms, treatment and outcomes and he related symptoms and treatments to outcomes. His best known study was the evaluation of blood letting as a treatment.

### BLOOD LETTING

Blood letting was standard practice in medicine for over 2500 years and reached its zenith in the mid 1800s. It was performed either by cutting a vein (or, less commonly, an artery) with a lancet, by using leeches to suck blood from a localized area, or by "cupping", a procedure to draw the blood to the localized skin surface. In just one year (1833) it is estimated that France imported 42 million leeches,<sup>4</sup> and it has been estimated that up to five million litres of blood were removed annually during the mid 1800s in France by leeches alone.<sup>5</sup>

It has been suggested that the first President of the United States, George Washington, died as a result of—or at least as a contribution of—blood letting. It has been estimated that up to 3.75 litres of blood were removed from the 68 year old ex-President over a period of about 10 hours.<sup>6</sup> That amount is over half of his blood volume. Other estimates report a lesser volume of blood loss, but most modern day physicians would agree that a patient with respiratory distress (Washington's primary symptom) would not benefit from becoming anaemic.

Blood letting was so popular that even by the late 1870s or 1880s physicians had to convince their patients not to be bled.

### PIERRE CHARLES ALEXANDRE LOUIS (1787–1872)

Pierre Charles Alexandre Louis was born into a lower class family in 1787 in Ai (or Ay), a small town in France. His

father was a wine merchant<sup>7</sup> but, due to the French Revolution (1789–1799), Pierre Louis was able to attend medical school in Paris. The French Revolution opened doors for the lower classes that were previously non-existent. He received his medical degree in 1813 and then went to Russia to practice medicine. After 6 years he returned to Paris, perhaps because he wanted an academic environment or intellectual stimulation.

At La Charité Hospital in Paris he gave himself the humble role of clinical clerk for several years, carefully observing and recording clinical facts, autopsy results and mortality, and cautiously generalizing based solely on these observed facts.<sup>8</sup> (pages 60–61)

### LA METHODE NUMERIQUE (THE NUMERICAL METHOD)

Louis collected records of many patient cases while at La Charité Hospital. He selected 77 cases of pneumonia and analysed them based on duration of disease and frequency of death stratified by time of first blood letting. He compared two groups, one bled during days 1–4 of their illness and the other bled during days 5–9 of their illness. (Note: His definition of pneumonia was recently found to be in agreement by 43 chest physicians in a study published in 2001.<sup>9</sup>) Of the patients bled within the first 4 days, 44% (18/41) died, compared with 25% (9/36) of those bled later. Louis acknowledged that the patients bled later may have already passed the peak or the worst phase of their disease, and thus had a better prognosis. He concluded that blood letting was useless in the treatment of pneumonia.

With regard to his "numerical method", Louis stated that "counting is not easy". He said: "It is necessary to account for the different circumstances of age, sex, temperament, physical condition, natural history of the disease, and errors in giving therapy". "The only reproach which can be made to the numerical method is that it offers real difficulties in its execution ... this method requires much more labor and time than the most distinguished members of our profession can dedicate to it."<sup>10</sup>

Louis wrote: "In any epidemic ... let us suppose 500 of the sick, taken in the same manner, to be subjected to one kind of treatment, and 500 others, taken in the same manner, to be treated in a different mode. If the mortality is greater among the first than among the second, must we not conclude that the treatment was less appropriate or less efficacious in the first class than in the second? ... It is impossible to appreciate each case with mathematical exactness, and it is precisely on this account that enumeration becomes necessary. By so doing the errors (which are inevitable) being the same in both groups of patients subjected to different treatment, mutually compensate each other, and they may be disregarded without sensibly affecting the exactness of the results."<sup>11</sup>

In a primer on evidence based medicine (EBM), Williams<sup>12</sup> states that EBM "requires an understanding of critical

appraisal and the basic epidemiologic principles of study design, point estimates, relative risk, odds ratios, confidence intervals, bias, and confounding". "Evidence-based medicine allows analysis of complicated material so that we can make the best possible clinical decisions for the populations we serve." Louis would concur.

How would the two other approaches to medical reasoning address this question? In 1793 there was a great yellow fever epidemic in Philadelphia. The physician Benjamin Rush (1745–1813) came to believe he could cure this disease with massive blood letting. He treated himself this way and survived the disease. What better source of empirical evidence? However, his proposed treatment called for the removal of 75% of the patient's total blood volume. The experimental physiologist might have removed 75% of the blood from an animal and observed the fatal results. Rush is a hero as a signatory of the American Declaration of Independence, but in 1793 he did more harm than good. Powell<sup>13</sup> describes Rush as "a ready victim of every trap self-discretion could lay" who found security in the good opinion of others. He kept his theory of treatment and ignored the facts. "He recognized no error except in others."

Thus we have three approaches to medical knowledge—the clinical judgement of the empirics and Benjamin Rush, experimental physiology of the Paris School, and the quantitative clinical correlations of Louis.<sup>14</sup> Proponents of these three approaches still continue to criticize each other.

*Clinical judgement* gets too little respect today. There are things that human beings do particularly well. One is pattern recognition. An experienced internist can tell someone has Cushing's disease by looking at them. The trained physician's eye sees characteristics of people's health which others do not see. To put it another way, computers cannot tell the difference between a cat and a dog but people can. Clinicians criticized Louis' method as taking too much time for the busy practitioner. It ignores the uniqueness of each patient by aggregating large numbers. Clinicians often criticize the experimental physiology for its lack of immediate relevance to patient care.

*Experimental physiologists* turned "empiricism" into a dirty word in medicine and it is defined as "quackery" in *Dorland's Medical Dictionary*. This criticism is levelled both at clinical reasoning and Louis' correlations which can be completely devoid of any theory. Today's reports of a drug trial showing that drug A is better at treating hypertension are devoid of any physiological theory. The value of a well controlled experiment is that there is no variation in the result and therefore no need for statistical tests of significance. Variation in outcome is proof that the experimental control is inadequate. Louis' mathematical approach can only show causation by the use of time (treatment precedes outcome) while the physiological experimental design demonstrates causation.

*Louis' mathematical method* might now be described as clinical epidemiology<sup>15</sup> and the foundation of evidence-based medicine.<sup>16–18</sup> His approach was correlational and not experimental, and now requires ruling out chance as an explanation for differences observed. Louis' followers criticize clinical judgement as being influenced by a variety of human biases. They would criticize the experimental physiologists for two reasons: (1) animal models may not be relevant for humans; and (2) treatments derived from physiological theory still need clinical evaluation to demonstrate efficacy. The sequence of steps used to bring a new drug to market thus moves from the laboratory to the clinical setting.

The careful listener in a big medical center can hear and see these three approaches in use. Instead of joining only one of these three hostile camps, we should come to appreciate the strengths and limitations of each.

## LOUIS AS CHANGE AGENT

Followers of this Heroes and Martyrs series realize that the three parts of quality improvement—patient focus, statistical mindedness and change agency—are considered. Louis' careful factual observation of patients and his use of mathematics have been mentioned. As a change agent he used two of the most powerful methods: he published his results and he taught and convinced good students.<sup>19–21</sup> While his conclusions were ignored by many of his busy colleagues, his students did hear him. Many of his students were from outside France, and many later returned to their native countries. His students formed the Society for Medical Observation in Paris, and several went on to demonstrate leadership and innovation by founding organizations or propagating new ideas. Louis' observations, teachings, and applications were thus widely disseminated. One student, William Farr (1807–1883), introduced several key epidemiology concepts such as herd immunity, dose-response, death rate, and cohort effect. Farr and two other students of Louis (William Guy and William Budd) founded the Statistical Society of London in 1834. Farr was a major reformer of public health and he noted the correlation between social-economic class and disease. In 1832 a group of Louis' students formed the Society for Medical Observation in Boston, USA. Two other students of Louis, Oliver Wendell Holmes and George Shattuck Jr, along with Shattuck's student Edward Jarvis, founded the American Statistical Society in 1851.<sup>7 8 22</sup>

As long as one is willing to wait a generation, teaching students is the way to change the world.

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## LETTER.....

### Real time patient safety audits

Real time patient safety audits undertaken by Ursprung *et al*<sup>1</sup> are potentially a novel approach to quality in health care and an interesting application of safety adapted from industry. From an error detection perspective they offer similar advantages to other prospective studies which had greater detection accuracy than retrospective medical record reviews.<sup>2</sup> The advantage of detecting errors before they occur, as opposed to mandatory or voluntary reporting which has delayed patient and time consequences, is perhaps the greatest strength of real time audits.<sup>1</sup> Real time audits should be able to assist in the development of systems with buffers and redundancy to decrease the likelihood of errors.<sup>1 3</sup>

Although the pilot program appears to have worked successfully, the longer term ambitions of the researchers to “develop a streamlined random safety audit tool for use by front line clinical staff without the need for additional personnel” needs to be considered with caution.<sup>1</sup>

The authors have made reference to the adoption of this technique from industry; however, what must be considered is that the success of industry has related to continued top up commitment including senior level leadership, dedicated personnel, and financial resources.<sup>4</sup> Real time problem solving has worked in industry because safety is a core value which is entrenched in the culture.<sup>4</sup> In order for health care to replicate similar culture changes, support and resources are needed. Limiting the resources available for the audits is likely to result in reduced success. Intercollaboration is needed to develop system changes, and the empowerment of individuals to feel they have resources to change and solve problems is essential in creating safety systems in healthcare organizations.<sup>4</sup> These areas are likely to suffer if inadequate support and resources are given.

Finally, common disadvantages of criteria audits that can also be applied to this study are the focus on process issues and lack of attention to interpersonal care.<sup>5</sup> Patient satisfaction is considered critical in measuring quality and ought to be considered alongside safety audits.<sup>6</sup>

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