Huth EJ (2006). Transatlantic ideas on the philosophy of therapeutics in the middle of the 19th century.

© Edward Huth, 1124 Morris Avenue, Bryn Mawr, PA 19010-1712, USA. E-mail: ejhuth23@verizon.net

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Early in the 19th century the move toward seeking numerical evidence in support of judgments on the efficacy of treatments advanced sharply with Pierre-Charles-Alexandre Louis' advocacy of *la méthode numérique* (the numerical method) through his case studies of blood-letting as a treatment (Louis 1836). This movement had begun prominently in the preceding century with Jurin's collection of numerical data on mortality from smallpox inoculation (Jurin 1724), Lind's trial on the treatment of scurvy (Lind 1753), and various British calls for numerical evidence on treatments (Tröhler 2005). But Louis' strong advocacy provoked passionate debates in the Académie des Sciences in Paris, which had their own important consequences. Among these was the publication in 1840 of *Principes Généraux de Statistique Médicale* by Jules Gavarret (Gavarret 1840).

In Chapter III of his *Principes*, Gavarret set forth explicit, detailed criteria for endeavouring to ensure that the characteristics of different groups of patients receiving different treatments (such as had been assembled for comparison by Louis) were sufficiently similar to allow confident inferences about effects of treatment. But more important in Chapter III from our perspective today was Gavarret's approach to inferential statistics for conclusions about the value of a treatment. He was critical of Louis' simply taking a single mortality datum as conclusive evidence for a judgment on the superiority of a treatment, demonstrating (Gavarret 1840, p 140-142) that Louis' mortality rate after treatment of 140 cases of typhoid fever could not be taken to be simply the 37% he reported from those cases but could, in other circumstances with 140 cases, range from 26% to 49%. Gavarret then goes on in his text to apply his time's equivalent of the calculation of confidence intervals (the probability calculation of "limits of oscillation") to examples of mortality data for two different treatments of the same disorder (Gavarret 1840, p 155-161) to indicate the degree of certainty one could apply to a conclusion of the superiority of one treatment over the other from those data.

Gavarret's book received the attention of many Europeans (Matthews 1995), some welcoming his analytical approach, others dismissing it. But it appears to have received little, or no, attention in the United States except for that of Elisha Bartlett, in his *An Essay on the Philosophy of Medical Science* (Bartlett 1844; Stempey 2005). How did Bartlett, this distant American, come to link his views to those of Gavarret?

Bartlett's *Essay* was published four years after Gavarret's *Principes* and eight years after Bartlett's year in Paris. The *Essay* is a complex work with a wide perspective on applications of scientific thinking and method in many aspects of medicine. Its 36 chapters are divided into two parts: *Part I, Philosophy of Physical Science* , which draws heavily on physics for principles underlying scientific thought, and *Part II, Philosophy of Medical Science* , in which Bartlett considers anatomy, physiology, pathology, diagnosis, and therapeutics in the light of the principles of science considered in Part I.

Most of what Bartlett says in Part I is unarguable, drawing as it does on the views of internationally eminent scientists who preceded Bartlett. But one part, with its ambiguity about the function or non-function of hypothesis in science, came up years later as vulnerable to adverse criticism. This section comes in Part I's Chapter IV, which opens with Bartlett's "Proposition Fourth".

> *A hypothesis is an attempted explanation, or interpretation, of these ascertained phenomena, and relationships, constituting science; and it is nothing else. It consists in an assumption, or a supposition of certain other unascertained, and unknown phenomena, or relationships. It does not constitute and [sic] essential element of science. All science is absolutely independent of hypothesis.*

As I shall comment later, twentieth-century medical historians have judged Bartlett's *Essay* to have been a major advance in thinking about evidence in therapeutics in its time, despite its failure to influence practice then. However, one American medical historian, Lester King, has been adversely critical of Bartlett's *Essay*, complaining that Bartlett failed to understand the importance of hypothesis in the

scientific method. But I think King (1991) paid too much attention to what appears to me to be Bartlett's critical view of hypotheses as the sole basis for judgments, such as those on the value of a treatment. Bartlett did concede farther along in this Chapter IV that an hypothesis could serve as a direction for research.

> *Without qualifying, in any degree, the doctrine which I have been endeavoring to elucidate, that all science is independent of hypothesis, I am quite willing to admit, that the hypothesis has often been of service to science, in suggesting, guiding and directing its researches. I am willing to go further than this … and to admit, at least the possibility … that the researches thus suggested and directed, may lead, ultimately, to the positive demonstration of the assumed phenomena, constituting the theory.*

But certainly Bartlett does not go further in Part I and discuss specifically how hypothesis might function in research in medicine. Bartlett's view in Part I was, in fact, echoed almost a century later by as an astute practitioner of clinical science as Thomas Lewis (Lewis 1920).

> *Except in those sciences which deal with the intangible or with events of long past ages, no treatises are to be found in which hypothesis figures as it does in medical writings. The purity of a science is to be judged by the paucity of its recorded hypotheses. Hypothesis has its right place, it forms a working basis; but it is an acknowledged makeshift, and, at the best, purpose unaccomplished. Hypothesis is the heart which no man with right purpose wears willingly upon his sleeve.*

For this commentary much of Part II is irrelevant to the history of calls for reliable evidence for judgments on treatments. The relevant sections come when Gavarret surfaces in Chapter XI of Part II with its specific consideration of statistical principles needed to decide on the certainty of a datum, in this case a numerical average (Bartlett's "an average result"). The page numbers given for the excerpts that follow are those in the original 1844 edition.

> *Let us now endeavour to see by* what method *… individual facts, phenomena, and relationships, can be generalized, so as to constitute the laws or principles of the science of life. … I have spoken of the law of the distribution of births between the two sexes. What is this law? and how is it ascertained? …. The true law of this proportion of the sexes at birth is seen [with extended investigation] gradually evolving itself from the study and analysis of a great* number of facts. … But [an] average result is not to be taken as the positive and absolute*. The result is still subject to a certain degree of variableness, or fluctuation; the amount of which can be ascertained by an arithmetical process, the elements of which are to be found in the numbers themselves, and which is known as the* calculation of probabilities. *(p 152-4).*

Here Bartlett is referring to Gavarret's *le calcul des probabilités* (probability calculation) for determining *les limites d'oscillation*, known in today's medical statistics as the confidence interval. In a footnote here Bartlett specifically credits Gavarret for the data on sex ratios at birth he uses to illustrate the principle he is developing.

A few pages later Bartlett takes up this principle as it should be applied to judgments on the efficacy of treatments.

> *Amongst these laws, there is no one of so much interest and importance, as that of the therapeutical relationships of disease; and there is no one, the determination of which requires a more rigorous adherence to the methods and conditions laid down in the foregoing pages. … I shall enter into a somewhat detailed exposition of the subject before us, in its connexion with therapeutics, or the treatment of disease; for the materials of which exposition, I am almost entirely indebted to the admirable treatise of M. Gavarret, on Medical Statistics. (p 159).*

This passage is followed by several pages on which Bartlett reviews the conditions set forth by Gavarret in his *Principes* that should be met to insure comparability of facts or phenomena.

> *The first condition, in the establishment of any therapeutical principle, or law, is this — that the facts, or phenomena, the relationships of which are to be investigated, shall be sufficiently fixed and definite to be* comparable*. The elements of this condition are thus stated by M. Gavarret. The subjects of the*

> *disease, whatever it is, which is to be studied, ought to be taken from the same locality, and from the same classes of population; and the hygienic circumstances surrounding these subjects, during the treatment of the disease, should also be the same. These precautions, it is easy to see, are necessary, in order to render the individual cases of disease* comparable. …
>
> *In the second place, the disease, to be studied, should be susceptible of a clear and positive diagnosis. … When the law that we are in search of is that of the effects of any given plan of treatment, upon any given disease, considered nosologically, or as a whole,* every case of the disease that presents itself*, should be taken into account, whatever may be its stage, its degree of severity, or its complications. There should be no selection of cases. ...*
>
> *In the third place, the method of treatment which is to be applied should be defined as distinctly and as clearly as possible. (p 158-62).*

These conditions, paraphrased here by Bartlett from Gavarret's 1840 statement of them in *Principes*, are, obviously, difficult to meet except in the most carefully designed and executed clinical trial. By the second half of the 20th century, the challenge of ensuring that like will be compared with like had been dealt with by the introduction of random allocation of patients to two or more treatment comparison groups.

Bartlett's restatement of Gavarret's conditions are followed by an emphasis on the necessity of studying large numbers of cases and of applying his use of the probability calculation to data gathered for judgments on treatments.

> *… The effects of the treatment upon the disease can result only from an examination and analysis of a* great number *of individual instances, and by an application to the average result, of the calculation of probabilities. The law, whatever it is, may be relied upon, as positive and absolute, just in proportion to the* fixed *and* uniform *character of the compared facts, and to the* greatness of their number *…. I shall conclude this portion of my subject with one or two illustrations, taken from the work of Gavarret, showing the necessity of an examination and analysis of* large numbers of cases*, in order to arrive at any safe or positive results in regards to the effects of any particular remedy, or mode of treatment, in any given disease; and the danger of receiving the average observed result of any given treatment, as the true expression of the law, in all cases where the number of instances is small. (p 164).*

That Bartlett drew so extensively in 1844 on Gavarret's *Principes* suggests strongly that he continued to read contemporary French medical literature after his return to the United States in 1827. There is no indication in his *Essay* that he relied on someone else's translation of *Principes*, so we must presume that he had a good command of French, probably based in large part on his 1826 year in Paris. This presumption is supported by his having translated from French in 1831 some of the biographical sketches of contemporary Parisian physicians and surgeons (Bartlett 1831) originally published in Paris by Jean Louis Hippolyte Peisse (1827-8).

Many pages later in *An Essay* comes evidence that he also paid close attention to British medical literature.

> *Even the rigorous numerical method of Louis, although it has been very slowly and reluctantly received into the modern medical mind of Great Britain, was adopted and followed, to a considerable extent, by some of her old observers, with whose names I have already graced these pages. Amongst these I may have mentioned particularly, Dr. Thomas Percival, of Manchester, who exhibits very strongly his fondness for positive numerical data, in a volume of* Medical Essays*, published as long ago as 1776; Dr. William Brown, of Edinburgh; William Woolcombe; John Chyne, in nearly all his Hospital Reports; and to these may be added, more recently, Dr. James Craufurd Gregory; Dr. David Cragie; Dr. William Henderson; Dr. John Reid, and Dr. Alexander P. Stewart. (p 303-4).*

In footnotes appended to some of these names, the dates of publications of some of these men make clear that at least some of these British physicians "thought numerically" well before Louis' strong advocacy of "the numeric method". But a remark a page earlier makes clear his opinion that British physicians up to his time, in general, did not think "numerically".

> *The principal defects of the British school are its want of comprehensiveness, of rigorous and positive conclusions, and the habit of mixing up, with its observations, reasonings and interpretations altogether hypothetical in their character; and then of regarding these reasonings as more important, more valuable, more essential to the constitution of science, than the observations upon which they are founded. (p 302).*

What influence did Bartlett's *Essay* have on his American contemporaries in medicine? If we judge by whether it stimulated systematic attention to gathering numerical data relevant to judgments on treatment and analyzing them for the certainty with which one could accept conclusions drawn from them, probably none, or, at least, very little. Much the same can be said of Gavarret's *Principes* for both American and European medicine. But if we can judge from William Osler's opinion rendered half a century later, many of Bartlett's contemporaries must have been impressed with his *Essay*, which would account for Osler's judgment (Osler 1928).

> An Essay on the Philosophy of Medicine*, 1844, a classic in American medical literature, is the most characteristic of Bartlett's works, and the one to which in the future students will turn most often, since it represents one of the most successful attempts to apply the principles of deductive reasoning to medicine, and it moreover illustrates the mental attitude of an acute and thoughtful observer in the middle of the century.*

Bartlett's *Essay* was reviewed in many American medical journals of the time (Stempey 2005, p 19-24) and, presumably, read by many of his contemporaries. His much later work, *The Philosophy of Therapeutics* , written about 1852, remained unpublished for many years. Fortunately it has been reconstructed by William E. Stempey from Bartlett's manuscript, now in a collection at the University of Rochester Library, Rochester, New York. Stempey's reconstruction is part of his truly comprehensive monograph, *Elisha Bartlett's Philosophy of Medicine* (Stempey 2005). This monograph includes not only Stempey's reconstruction of *Philosophy* … (Bartlett 2005), but also a re-publication of Bartlett's *Essay*, with the page numbers of the original version indicated in this modern version.

Bartlett must have remained concerned with the proper principles guiding judgments on treatments because he turned again close to a decade later to writing his for-years-unpublished *The Philosophy of Therapeutics* (Bartlett 2005). To a degree *Philosophy* repeats much of the same reasoning as *An Essay* but with perhaps sharper statements of its central points. Near its beginning he emphasizes that we — in his time — cannot determine from what we know of the origins and nature of a drug what causes its effects. Note that the page references for these excerpts are to Stempey's published reconstruction of *Philosophy*.

> *The natural history of cinchona, its botanical character and relations, its geographical distribution, its anatomy and physiology, its chemical constitution, do not involve in any way its therapeutical properties; they do not even indicate them, or throw any light upon them. (p 198).*

Much of this is no longer true; the development of pharmacology toward the end of the 19th century and the beginning of the 20th century began to throw light for many drugs on the relation between the chemical composition of a drug and its effects. A few pages later he sharpens points he made earlier in *An Essay* on the conditions needed to legitimatize conclusions about the efficacy of a treatment.

> *The first essential and fundamental condition of all therapeutical science, is to fix as far as possible, … its variable and fluctuating element. The problem to be solved is this: given a certain pathological condition or process, and a certain substance or agent, or a combination of substances and agencies of the* materia medica*,—to find the true relation between them,—to ascertain the changes effected in the former by the latter. … The more nearly the several individual cases of disease, with which we are dealing approach each other —the more exactly alike they are—the more nearly they represent equal quantities or forces, the more absolute and complete will our solution become. The means for securing as far as possible, this essential primary condition, may be briefly stated.*
>
> *First: The general hygienic conditions and history of the subjects of the diseases should be substantially the same. … It would not be safe, for instance, to compare any two modes of treatment of typhus, one mode tried upon the comfortable and educated classes—and the other upon the inmates of an alms house. Into what enormous error should we be led, in comparing two methods of treating pneumonia—one of them in cases of temperate, and the other in cases of intemperate subjects!*

> *Second: The subjects of the disease should be within certain limits, of the same age. Age is a very important element in the natural history of a disease. ...*
>
> *Third: The subjects of the disease should be of the same sex. …*
>
> *Fourth: There may be certain special conditions which are to be considered, for instance, the state of pregnancy. …*
>
> *Fifth: The general extent, severity, and character, of the cases, should be substantially the same. …*
>
> *Sixth: The period of the disease at which treatment is commenced, and during which it is continued should be substantially the same. …*
>
> *Seventh: The method of medication should be as simple as possible …*
>
> *Finally, after having fulfilled all these conditions, our observation must embrace an adequate number of instances. This adequate number will vary under different circumstances, and in different diseases; but in most cases, as a general rule, it must be large; and the larger the number the more positive and certain will our conclusions be. (p 201-2).*

These "conditions" clearly echo those Bartlett made in his *Essay*, where he credited Gavarret with the same perspective. His failure to credit Gavarret here may stem only from the unfinished character of the manuscript of *Philosophy*. Bartlett goes on to emphasize the importance of an observer's judging treatment results with no preconceived convictions and a fully open mind in considering the observations made.

> *… There are two … qualities essential to a competent and trustworthy observer, to which I refer. The first of these is what may be called scientific probity or integrity—truthfulness—supreme love of the truth; —unqualified and unswerving allegiance to the truth—whatever the scientific focus and consequences might be ...*
>
> *Closely allied to this is what may be called scientific indifference to the results of our observations, a quality of mind of most rare and difficult attainment, but most essential to the trusty and true observer. He must see clearly that the scientific truth he seeks is in nature—not in his thoughts or wishes—and that his sole function is to find where and what it is. The various passions of the human heart may dread or may desire, this issue or another: —but science asks one only question. And that is—What is? (p 201-3).*

In the rest of *Philosophy* Bartlett discusses in detail his view of the central principles that should be inherent in a science of therapy. He closes with unequivocal statements bearing his conviction that the central reason for medicine's existence is to treat the ill.

> *The science of medicine issues finally in the end of therapeutics. This is its consummation—its great end and purpose. Anatomy, physiology, pathology, —the entire natural history of disease—*materia medica*—all are preliminary, more or less direct and essential, for the cure or mitigation of disease. ... The great purpose of this study is to make the physician; and the physician is he who, within the limits and conditions of his science and art, prevents, mitigates, and cures disease. (p 211-2).*

Why did Bartlett not finish *Philosophy* and get it published? He died in 1855 at the end of an ill-defined illness with leg pains and difficulties in walking. One speculation ([Anonymous] 1904) was that he suffered from lead poisoning. Conceivably, he may have suffered from *tabes dorsalis*, which could account for both "paralysis" and leg pains, a tertiary manifestation of syphilis he might have acquired during his 1826 stay in Paris, but this diagnosis might not clearly account for his death. Some of the citations earlier in this commentary make clear his sterling reputation among contemporaries even if they were not influenced by his pioneering views on the evidence needed for judgments on treatments.

As commented above in discussing King's adversely critical view of *Essay*, judgments in the twentieth century of Bartlett's contributions in his *Essay* have generally been favorable. One, which I believe is characteristic of others, is that of Cassedy (1984).

> *The fullest American exposition of the numerical point of view in medicine*

> *was formulated by Elisha Bartlett in 1844 …. [He] did not simply restate the well-known concepts of Louis; he incorporated also the far more sophisticated numerical vision of Louis's Parisian contemporary, Jules Gavarret. Gavarret, several generations ahead of his time, had outlined in 1840 some of the potentialities for mathematics in medical-statistical analysis, including the calculus of probabilities.*

In calling for numerical evidence on the value of a treatment, it is clear that Bartlett simply had in mind assembling observations made on similar patients treated in different ways - what we might call matched cohort studies today. He did not, apparently, conceptualise developing a hypothesis about the relative merits of two different treatments, then designing a prospective trial comparing their effects. That kind of development did not begin until late in the 19th century, and did not find wide application until the second half of the 20th century.

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References

[Anonymous] (1904). Bartlett, Elisha (1804-1855). In: The national cyclopaedia of American biography, being the history of the United States. Volume 12. New York: James T. White & Co, p 70.

Bartlett E (1831). Sketches of the character and writings of eminent living surgeons and physicians of Paris. Translated from the French of J. L. H. P. Boston: Carter, Hendee and Babcock.

Bartlett E (1844). An essay on the philosophy of medical science. Philadelphia: Lea & Blanchard. Essay has been republished in Stempey's 2005 monograph; see the reference to Stempey (2005) below.

Bartlett E (circa 1852). The philosophy of therapeutics. In: Bartlett Family Papers http://www.lib.rochester.edu/index.cfm. Accessed 9 January 2006. This collection contains many letters from and to Elisha Bartlett, and notably, the unpublished manuscript of Philosophy of Therapeutics.

Bartlett E (2005). The philosophy of therapeutics. In: Stempey WJ (2005). Elisha Bartlett's philosophy of medicine. Dordrecht, The Netherlands: Springer. P 197-212. Stempey judges from manuscript evidence that Bartlett probably wrote this work about 1852.

Cassedy JH (1984). American medicine and statistical thinking, 1800-1860. Cambridge, Massachusetts: Harvard University Press, p 66-7.

Gavarret J (1840). Principes généraux de statistique médicale ou développement des règles qui doivent présider à son emploi. Paris: Bechet Jeune et Labé.

King LS (1991). Transformations in American medicine: From Benjamin Rush to William Osler. Baltimore: Johns Hopkins University Press.

Lewis T (1920). The mechanism and graphic registration of the heart beat, p vii. Cited in: Bynum WF, Porter R (2005). Oxford dictionary of scientific quotations. Oxford: Oxford University Press, p 384.

Louis PCA (1836). Researches on the effects of bloodletting in some inflammatory diseases: and on the influence of tartarized antimony and vesication in pneumonitis. Translated by CG Putnam; with preface and appendix by James Jackson. Boston: Hilliard, Gray & company.

Matthews JR (1995). Quantification and the quest for medical certainty. Princeton, New Jersey: Princeton University Press.

Osler W (1928). Bartlett, Elisha (1804-1855). In: Kelly HA, Burrage WL eds. Dictionary of medical biography: Lives of eminent physicians of the United States and Canada, from the earliest times. New York: D Appleton, p 65-6.

Peisse JJH (1827-8). Les médecins français contemporains. Paris: Librairie de l'industrie.

Stempey WJ (2005). Elisha Bartlett's philosophy of medicine. Dordrecht, The Netherlands: Springer.

Tröhler U (2005). Quantifying experience and beating biases: A new culture in eighteenth-century British clinical medicine. In: Jorland G, Opinel A, Weisz G, eds. Body Counts: Medical quantification in historical and sociological

perspective. Montreal, London, Ithaca: McGill University Press. p 19-50.