New observations support William Osler's rationale for systemic bloodletting

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ABSTRACT

Bloodletting has been called William Osler's "blind spot," especially with respect to pneumonia. Also puzzling has been his endorsement of bleeding in selected cases of heatstroke. Recent clinical observations on pneumonia and, to a lesser extent, heatstroke lend support to Osler's rationale for bloodletting in these conditions. A 21st-century rationale now exists for all eight indications for systemic bloodletting listed by Osler in the first edition of his textbook, *The Principles and Practice of Medicine* (1892): treatment of acute heart failure (seven of the eight indications) or rapid lowering of blood pressure (in subarachnoid hemorrhage accompanied by severe hypertension). These observations support the narrative that during Osler's lifetime, bloodletting became more "rational" largely on the basis of cumulative clinical experience.

KEYWORDS Bloodletting; heart failure; heatstroke; William Osler

Therapeutic bloodletting dates to antiquity and lends to opposing narratives. For some, bloodletting epitomizes dangerous practices of yesteryear. For others, including some medical historians, doctors bled because it sometimes worked, and over time bleeding became more "rational." Both narratives are partly correct, with a dividing line somewhere between 1830 and 1870.^{1–6} Lewis Thomas probably had bloodletting in mind when he wrote: "It was discovered, sometime in the 1830s, that the greater part of medicine was nonsense."⁷

Pneumonia has been a stumbling block to those seeking to clarify the rationale for bloodletting, for physicians of yesteryear and historians down to the present time. Mentioned in this context is Sir William Osler (1849–1919), who, in the first edition of *The Principles and Practice of Medicine* (1892), endorsed systemic bloodletting (phlebotomy, then known as venesection) for eight conditions.⁸ These endorsements, especially for pneumonia, have puzzled observers through the years to the extent that Michael Bliss, Osler's most recent biographer, called it "a blind spot."⁹ The purpose of this article is to review Osler's recommendations, taking into account recent clinical observations.

BACKGROUND

Prior to 1830, enthusiasm for bloodletting ebbed and flowed as "systems" of disease causation came and went. In the 18th century, John Brown (1735–1788) of Edinburgh proposed that living tissues are "excitable" and diseases are either *sthenic* (increased excitement) or *asthenic* (decreased excitement). Brown considered most diseases asthenic and therefore used stimulants rather than depletory measures such as bleeding and purging. Benjamin Rush (1745–1813) of Philadelphia concluded from the 1793 yellow fever epidemic that diseases had become "sthenic" and to that end popularized venesection in the US.^{10,11} Others did likewise in Europe.

Historians credit Pierre-Charles-Alexandre Louis (1787–1872) of Paris for stemming the tide of unnecessary bloodletting. Between 1828 and 1835, Louis applied his "numerical" method (statistics) to bloodletting, especially for pneumonia, and although his findings were not entirely clear-cut they carried weight.¹² Pupils of Louis such as Marshall Hall (1790–1857) in England and a cohort of young Americans who had studied in Paris joined the fray. By the 1850s the old "heroic" therapy had been largely abandoned by many, and perhaps most, physicians chiefly on the basis of clinical experience, therapeutic skepticism, the introduction of new remedies,

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Figure 1. Recommendations for bloodletting for nine selected indications (chosen for consistency of nomenclature) according to US textbooks of medicine published between 1830 and 2004.^{8,20–32} The methods for rating the strength of recommendation of bloodletting on a 0 to 4 scale (that is, *never* to *most cases*) are shown in the appendix to a previous article.¹⁹

the advent of rival schools such as homeopathy, and thought leaders such as Jacob Bigelow (1787–1879), whose *Discourse on Self-Limited Diseases* (1835) proved highly influential.^{13,14} To explain why they no longer bled, some doctors invoked the “change of type” theory, which held that disease, people, or both had changed from a sthenic to an asthenic type.¹⁵

In 1859, William Orlando Markham (1818–1891), in an address to the Royal Medical and Chirurgical Society of Great Britain, concluded that the major benefit of bleeding was relief of “cardiopulmonary congestion.”¹⁶ This was roughly the equivalent of “heart failure,” a term that did not come into wide use until the 20th century.¹⁷ Phlebotomy for acute heart failure, and especially for pulmonary edema, is eminently reasonable from a 21st-century perspective as a way to reduce blood volume should potent diuretics be unavailable.¹⁸ Thereafter, recommendations for bloodletting rapidly fell off for most conditions that did not involve “cardiopulmonary congestion.”

In 1964 the present author reported an analysis of bloodletting as advocated by authors of textbooks of medicine published between 1830 and 1892, the latter date chosen as the year Osler brought out his textbook.¹⁹ Those data have now been updated to include 14 representative US textbooks of medicine published between 1830 and 2004 (*Figure 1*).^{8,20–32} As shown in *Figure 1*, recommendations for bleeding were abandoned in medical textbooks between 1830 and 1892 for conditions for which there is no rationale by 21st-century criteria: acute meningitis, nephritis, and peritonitis. Bleeding was retained for acute pulmonary edema. Bleeding was also retained for cerebral hemorrhage—notably, subarachnoid hemorrhage accompanied by severe hypertension—as a way to lower blood pressure rapidly. Bleeding for pneumonia triggered the most controversy and equivocation.

In 1856 a bitter debate known to historians as “the Edinburgh bloodletting controversy” erupted in that city between newly arrived John Hughes Bennett (1812–1875) and William Pulteney Alison (1790–1859), the acknowledged dean of Edinburgh medicine.³³ The controversy largely concerned bloodletting for pneumonia. Alison favored it and Bennett opposed it. In the USA, Alfred Lebbeus Loomis (1831–1895) opposed bleeding for pneumonia in the 1885 edition of his textbook,³⁴ whereas Austin Flint (1812–1886) endorsed it in the 1894 edition of his textbook (published posthumously), and also in earlier editions, for cases in which there was “accumulation of blood in the cavities of the right side of the heart.”³⁵

The controversy about bloodletting for pneumonia continued well into the 20th century. Not until the 1940s was it rendered largely moot by antimicrobial drugs and other ways to treat pneumonia and its complications.

OSLER'S RECOMMENDATIONS FOR BLOODLETTING

Shown in *Table 1* are the eight indications for systemic bloodletting cited by Osler in the first edition of his textbook. The term heart failure was not then in common usage; in his textbook, Osler used it only in connection with diphtheria and typhoid.^{8,17} Observe, however, that Osler described symptoms and signs of acute heart failure in the first five of these indications: chronic valvular heart disease, arteriosclerosis, cardiac hypertrophy and dilatation, pulmonary edema, and emphysema with “great engorgement of the veins.” In cerebral hemorrhage, Osler’s rationale was “to reduce the arterial pressure.” In 1901, Osler’s close friend and younger colleague Harvey Cushing (1869–1939) demonstrated that an acute increase in intracranial pressure precipitates extreme hypertension, confirming Osler’s rationale.^{36,37}

Pneumonia is the only indication for which Osler made substantial changes in the wording of these recommendations in later editions of his textbook. In the first edition (1892), he wrote: “Pneumonia is one of the diseases in which a timely venesection may save life.”⁸ In the third edition (1898), he added that “the practitioner must ever be on the alert to prevent the onset of cardiac weakness, and to treat it should that condition arise.” In the eighth edition (1918), the last published during his lifetime and coauthored with Thomas McCrae, Osler was more specific: “Late in the course marked dilatation of the right heart is the common indication [for venesection]. The quantity of blood removed must be decided by the effect; small amounts are often sufficient.”²⁴ This wording is almost identical to the wording used by Austin Flint.³⁵ When Henry A. Christian assumed editorship of Osler’s textbook in 1938, he made it clear that bleeding remained useful in cases with pneumonia accompanied by cyanosis and distended neck veins, and he continued this advice through the 16th edition (1947) despite introduction of sulfonamides and penicillin.

Table 1. Indications and rationale for systemic bloodletting (phlebotomy; venesection) in the first edition of *The Principles and Practice of Medicine* (1892), by William Osler⁸

Indication	Rationale
Chronic valvular heart disease (p. 624)	"In cases of dilatation, from whatever cause, whether in mitral or aortic lesion or distention of the right ventricle in emphysema, when signs of venous engorgement are marked and when there is orthopnoea with cyanosis, the abstraction of from twenty to thirty ounces of blood is indicated. This is the condition in which timely venesection may save the patient's life. It is the condition in which I have had most satisfactory results from venesection. It is done much better early than late. I have on several occasions regretted its postponement, particularly in instances of acute dilatation and cyanosis in connection with emphysema."
Arterio sclerosis (p. 679)	"In cases which come under observation for the first time with dyspnoea, slight lividity, and signs of cardiac insufficiency, venesection is indicated. In some instances, with very high tension, striking relief is afforded by the abstraction of twenty ounces of blood."
Cardiac hypertrophy and dilatation (p. 640)	"... with signs of dilatation, as indicated by gallop rhythm, urgent dyspnoea, and slight lividity, venesection is in many cases the only means by which the life of the patient may be saved, and from twenty-five to thirty ounces of blood should be abstracted without delay."
Pulmonary edema (p. 506)	"The treatment of oedema of the lung is practically that of the condition with which it is associated. In the acute cases active catharsis, and, if there is cyanosis, free venesection should be resorted to."
Emphysema (p. 549)	"Patients who come into the hospital in a state of urgent dyspnoea and lividity, with great engorgement of the veins, particularly if they are young and vigorous, should be bled freely. On more than one occasion I have saved the lives of persons in this condition with venesection."
Cerebral hemorrhage (p. 882)	"The patient should be placed with head high, and measures immediately taken to reduce the arterial pressure. Of these the most rapid and satisfactory is venesection, which should be practiced whenever the arterial tension is much increased."
Pneumonia (p. 530)	"In many cases the question comes up at the onset [of pneumonia] as to the propriety of venesection. ... Pneumonia is one of the diseases in which a timely venesection may save life. To be of service it should be done early. In a full-blooded, healthy man with high fever and bounding pulse the abstraction of from twenty to thirty ounces of blood is in every way beneficial, relieving the pain and dyspnoea, reducing the temperature, and allaying the cerebral symptoms, so violent in some instances. Unfortunately, in a majority of the cases, bleeding is now used at a late stage in the disease, when the heart is beginning to fail, the right chambers are dilated, the face is of a dusky hue, the respirations are very rapid, and there are signs, perhaps, of oedema of the uninvolved portions of the lungs. Though resorted to rather as a forlorn hope, it is a rational practice, and, in cases of emphysema and of heart-disease, proves satisfactory under identical hydraulic indications, but, unfortunately, in a majority of the cases of pneumonia it proves futile. Time and again, in such cases, have I urged free venesection, but in twelve hospital patients bled under these circumstances only one recovered."
Sunstroke (heatstroke) (p. 1018)	"In the cases in which the symptoms are those of intense asphyxia, and in which death may take place in a few minutes, free bleeding should be practised, a procedure which saved Weir Mitchell when a young man."

For sunstroke (heatstroke), Osler never altered the wording of his recommendation for bleeding in select cases, especially because the procedure "saved Weir Mitchell when a young man" (*Table 1*). Silas Weir Mitchell (1829–1914), Osler's older colleague in Philadelphia, went on to a distinguished career as a neurologist and also as a writer.

PNEUMONIA

Osler and others, including Flint and Christian, thus considered the primary indication for bloodletting in pneumonia to be acute heart failure. The problem back then was how to determine which patients might benefit, especially because symptoms and signs of pneumonia and heart failure overlap. Recent observations shed light on Osler's rationale.

To be sure, the clinical spectrum of community-acquired pneumonia (CAP) during Osler's lifetime was not the same as

it is today. Osler dealt mainly with lobar pneumonia due to *Streptococcus pneumoniae*, which during his era was often seen in younger, previously healthy adults. That scenario is now uncommon; the spectrum of recognized pathogens in CAP is now much broader, and the disease predominantly affects the elderly and debilitated. We should also mention that Osler did not recognize acute myocardial infarction as a complication of pneumonia. It was not until 1912 that James B. Herrick published his classic paper on myocardial infarction,³⁸ and Osler was slow to adopt the electrocardiogram.³⁹

With these caveats, recent observations on the frequency of cardiac complications of pneumonia strongly support the rationale given by Osler, Flint, and others for bloodletting in selected cases of pneumonia, namely, treatment of acute heart failure.

Population-based studies suggest that heart failure increases mortality from CAP by up to 50%, especially among the elderly.^{40–42} A clinical study of 130 patients

suggested an even greater effect of cardiac complications on mortality in patients with CAP (21.8% vs 6.1%, $P < 0.05$).⁴³ In 2007, Musher and colleagues reported that 33 (19.4%) of 170 patients with pneumococcal pneumonia experienced one or more major cardiac events, such as new or worsening heart failure (24 patients), myocardial infarction (12 patients), and/or new arrhythmia (10 patients).⁴⁴ In January 2019, Musher and colleagues confirmed the substantial risk of acute myocardial infarction in pneumonia, which peaks at the onset of illness and correlates with severity of pneumonia. Reviewing the literature, they concluded that this association holds for pneumonia from any cause, not just pneumococcal disease.⁴⁵

A few investigators have explored the use of routine transthoracic echocardiography to predict complications from CAP. From a study of 111 consecutive adults with CAP, it was concluded that patients with abnormal tricuspid annular plane systolic excursion, taken as a measure of right ventricular systolic function, have a worse prognosis.^{46,47} From a study of 75 consecutive adults with CAP, it was concluded that changes in pulmonary artery systolic pressure correlate with radiographic severity and peripheral oxygenation.⁴⁸ From a study of 234 patients with acute respiratory distress syndrome (ARDS) from any cause, it was concluded that echocardiographic demonstration of acute severe cor pulmonale predicts mortality.⁴⁹ Osler's account of late stages of pneumonia in which "the heart is beginning to fail, the right chambers are dilated, the face is of a dusky hue, the respirations are very rapid, and there are signs, perhaps, of oedema of the uninvolved portions of the lungs" (*Table 1*) could possibly be taken as an early description of ARDS.

HEATSTROKE

Osler's anecdote that bleeding "saved Weir Mitchell when a young man" when the future neurologist suffered heatstroke is a bit puzzling. However, pulmonary edema is well recognized as a complication of heatstroke, "occasional" or "common" according to different authors. The proposed pathogenesis, which appears to be better studied in dogs than in humans,⁵⁰ involves combinations of high-output cardiac failure, suppression of myocardial function, fluid overload from acute renal failure, fluid overload from overly aggressive rehydration, ARDS, and systemic inflammatory response with cytokine storm. The take-home point from recent discussions of pulmonary edema in heatstroke is that physicians should take care to avoid fluid overload in a situation that usually calls for aggressive rehydration.^{50–56}

PERSPECTIVE

Although information and data presented here support the narrative that bloodletting became more "rational" during Osler's lifetime, we should clarify four points. First, Osler made no unique contributions in this area. His opinions largely reflect those of his era's leading clinicians. Second, despite his alleged therapeutic nihilism, Osler was usually willing

to prescribe what worked or might work. Third, Osler's endorsement of local (topical) bloodletting by cupping or application of leeches merits brief mention. His indications for topical bloodletting included acute pericarditis with effusion, for which he never changed the wording in his textbook. Finally, we should point out that Osler's recommendations in his textbook may have differed from what he actually did for sick people. In a previous paper, the present author showed that what doctors did in daily practice often varied substantially from textbook recommendations; then as now, physicians often based treatment on judgment, personal experience, and prevailing style of practice.¹⁹ In 1875, Samuel D. Gross (1805–1884), a leading US surgeon, commenting on how doctors no longer bled in situations where it might help, said that "the fate of blood-letting ... shows what little faith there is to be placed in human judgment, and how sadly we are influenced by authority and fashion in a matter pertaining to the dearest interests of society."⁵⁷

Bloodletting is perhaps the world's longest-running observational therapeutic trial, although indications keep changing. Polycythemia vera was added to the short list of indications during Osler's lifetime, and phlebotomy is now a treatment of choice for hemochromatosis and porphyria cutanea tarda (*Figure 1*). Proposed new indications for bloodletting still crop up. Perhaps the most intriguing proposal in recent years concerns metabolic syndrome, a highly prevalent but poorly understood condition with obesity, glucose intolerance, insulin resistance, hypertension, and dyslipidemia. From a randomized, controlled, single-blind trial involving 64 patients with metabolic syndrome, it was concluded that phlebotomy reduced systolic blood pressure, heart rate, blood glucose levels, hemoglobin A1c levels, and low-density lipoprotein/high-density lipoprotein ratios.⁵⁸ These observations, if confirmed, would benefit blood banks and validate the old English adage, "A bleeding in the spring, is physic for a king."

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