

Teaching fever aphorisms: Osler revisited

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Sir William Osler was a master clinician, renowned for his clinical method, attention to detail, and his diagnostic acumen. In Osler's era, infectious diseases were rampant and Osler had the opportunity to observe and write about many infectious diseases that he encountered at the time. In his famous *Textbook of Medicine*, published in 1892, pride of place goes to infectious diseases, and the infectious disease section begins with 39 pages devoted to typhoid fever. Because diagnostic tests available at the time were limited, Osler based his diagnoses on a careful analysis of the patient's febrile response and correlated that with the clinical findings to arrive at a diagnosis. Osler was able to correctly diagnose infectious diseases with similar presenting symptoms based on his careful analysis of the patients' fever curves. He was also careful to note the relationship of each patient's pulse to fever [1, 2].

In the 1850s, the most important differential diagnostic problem in infectious disease was the differentiation of typhoid fever from malaria. Most clinicians at the time were so confused by the similarity of symptoms of these disorders that the diagnosis of "typhomalaria" was used. "Typhomalaria" was a testimony to the lack of attention being paid to the details of fever curves associated with typhoid fever compared to those of malaria [3–5].

Osler not only appreciated that relative bradycardia was a cardinal sign of typhoid fever, he also understood the

temporal relationships between relative bradycardia and the natural history of the infection. In the medical literature today, many authors report that relative bradycardia is not often present in typhoid fever and therefore is a less reliable diagnostic finding than previously described [1, 6]. Osler was careful to note that relative bradycardia occurred late rather than early in the natural history of typhoid fever. Today, we rarely have the opportunity to observe the untreated natural course of an infectious disease for more than a few days because of economic constraints on length of stay for hospitalized patients. However, this does not detract from the validity of his observations and it accounts for the discrepancy between his and contemporary descriptions of the incidence and diagnostic importance of relative bradycardia in typhoid fever [7, 8].

Osler solved the "typhomalarial" diagnostic dilemma by carefully comparing the fever curves and pulse relationships of these two different infectious diseases, thereby debunking "typhomalaria" forever. He also noted that coinfection is rare; patients have either typhoid fever or malaria and rarely, if ever, both simultaneously [1, 8]. Clinicians today often lament the excesses and undue reliance on diagnostic testing at the expense of careful diagnostic methods at the bedside. The lack of careful observation and diagnostic reasoning skills all too often lacking in some house officers is regrettable but, in part, it is the fault of many training programs. More time is spent ordering CT scans than in analyzing the patient's fever curves and correlating them with clinical findings. How many hours of house staff core lectures or conferences throughout the academic year are devoted to the diagnostic significance of fever? If included in core lectures, fever of unknown origin, or the pathophysiology of fever are the topics covered most often. House officers are faced with diagnosing acute fevers in their hospitalized patients every

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day, yet they receive little teaching on the diagnostic approach to acute fevers. Fever aphorisms are rarely repeated or used on ward rounds.

From an analysis of the height of the fever, its periodicity/characteristics and relationship to the pulse, much important diagnostic information can be garnered to differentiate noninfectious from infectious disorders. Fever aphorisms can narrow diagnostic possibilities and often result in a presumptive clinical diagnosis [9, 10]. Fever curves per se have not been shown to be very useful in contemporary medical practice [11]. The classic descriptions of fever curves in the literature were based on a limited number of infectious diseases. Sometimes, fever curves were the only way to make a diagnosis in cases when the usual diagnostic modalities were unhelpful, i.e., the double quotidian fever of adult juvenile rheumatoid arthritis (Still's disease) or kala-azar [9, 10].

The magnitude of the fever alone has important diagnostic significance. Temperatures $\geq 106^\circ\text{F}$ (41.1°C) are rarely related to infection and almost always indicate a noninfectious disorder, i.e., central fevers, drug fever, malignant neuroleptic syndrome, malignant hyperthermia, heatstroke. As extreme hyperpyrexia has diagnostic significance, so does hypothermia. Hypothermia indicates an inadequate host response to infection and has negative prognostic significance. Hypothermia is commonly observed in patients with chronic renal failure and systemic infection and in cases of alcoholic cirrhosis with advanced liver disease. Considerable healthcare resources could be saved if more physicians appreciated that a single, isolated fever spike in a hospitalized patient occurs rarely, if ever, on an infectious basis. Excluding procedure-related transient bacteremias or blood-product transfusions, isolated fever spikes ($102\text{--}104^\circ\text{F}$; $38.9\text{--}40.7^\circ\text{C}$) are not associated with systemic infections [9, 10].

Most noninfectious disease disorders accompanied by fever are accompanied by temperatures $\leq 102^\circ\text{F}$ (38.9°C). There are important exceptions to this rule; noninfectious disorders that may have temperatures $\geq 102^\circ\text{F}$ (38.9°C) include systemic lupus erythematosus (SLE), drug fevers, renal cell carcinomas, lymphoreticular malignancies, thyroid storm, acute adrenal insufficiency, etc. Since most noninfectious disorders produce temperatures $< 102^\circ\text{F}$ (38.9°C), most infectious diseases have the potential for temperatures $\geq 102^\circ\text{F}$ (38.9°C). The "102°F rule" is best used in the differential diagnosis for similar disorders, i.e., acute cholecystitis versus cholangitis, cystitis versus acute pyelonephritis, pulmonary emboli versus septic pulmonary emboli, phlebitis versus septic thrombophlebitis, etc [9, 10].

The importance of the pulse-to-temperature relationship is particularly underappreciated. Pulse and temperature are physiologically related, i.e., for every degree of temperature elevation (degrees Fahrenheit), there is a commensurate in-

crease in the pulse rate of 10 beats/minute. Excluding patients with arrhythmias, pacemaker rhythms, those on β -blockers, diltiazem, or verapamil, a pulse rate lower than that appropriate for a given degree of temperature is termed relative bradycardia. Therefore, a patient with a temperature of 105°F (40.6°C) should have a pulse of approximately 140 beats/minute. Even if such a patient has a rapid pulse of 120 beats/minute, a pulse-to-temperature deficit is present and should be considered as relative bradycardia. Relative bradycardia has important diagnostic significance in febrile patients [9, 10–12].

As clinicians, we need to re-emphasize the importance of the differential diagnostic implications of fever. By applying Osler's careful attention to detail, the correct diagnosis can be made more rapidly and will result in focused diagnostic testing, thereby saving the patient unnecessary procedures and conserving hospital resources. Patients with drug fevers are a prime example. It is estimated that as many as 10% of hospitalized patients with fever have a drug fever. If a drug fever is not considered in the differential diagnosis and its characteristic features are missed, patients are often subjected to unnecessary empiric therapy, diagnostic tests, consultations and prolonged length of stay, while the hospital incurs increased costs.

By careful bedside consideration of the aspects of fever and by correlating them with the clinical findings, Osler is indeed revisited. While fever curves are unhelpful with some fevers related to medical progress, such as central intravenous line infections, nosocomial endocarditis, ventilator-associated pneumonias, balloon pump fevers, analysis of *C. difficile* colitis, etc., the analysis of fever characteristics still has merit. By incorporating the diagnostic aspects of fever in differential diagnoses in lectures and rounds, we continue a long tradition of work by master infectious disease clinicians. If we do not more actively emphasize the fever component of infections, future generations of clinicians will fail to appreciate the diagnostic importance of fever and relegate fever aphorisms to a historical footnote. In the Oslerian tradition of careful observation and bedside clinical correlation, as infectious disease teachers and clinicians we should renew our efforts to teach the diagnostic significance of fever to house staff. Fever is still a hot topic. Back to fever aphorisms at the bedside; Osler would be most pleased.

References

1. Osler W (1892) Typhoid. In: The principles and practices of medicine. Appleton, New York, pp 2–39
2. Osler W (1899) The diagnosis of typhoid fever. *New York Med J* 70:673–676
3. Richens J (1996) Typhoid fever. In: Cox FEG (ed) Illustrated history of tropical diseases. Wellcome Trust, London, pp 25–39

4. Osler W (1892) Malaria. In: *The principles and practices of medicine*. Appleton, New York, pp 141–157
5. Osler W (1897) The diagnosis of malarial fever. *Med News* 70:289–292
6. Cunha BA (2005) Malaria or typhoid fever: a diagnostic dilemma? *Am J Med* 118:1442–1443
7. Cunha BA (2006) Typhoid fever: the temporal relations of key clinical diagnostic points. *Infect Lancet* 6:318–320
8. Cunha BA (2004) Osler on typhoid fever: differentiating typhoid from typhus and malaria. *Infect Dis Clin North Am* 18:111–125
9. Woodward TE (1991) The fever pattern as a clinical diagnostic aid. In: Mackowiak P (ed) *Fever: basic mechanisms and management*. Raven, New York, pp 84–103
10. Cunha BA (1996) The clinical significance of fever patterns. *Infect Dis Clin North Am* 10:33–44
11. Musher DM, Fainstein V, Young EJ, Pruett TL (1979) Fever patterns: their lack of significance. *Arch Intern Med* 139:1225
12. Cunha BA (2000) The diagnostic significance of relative bradycardia in infectious disease. *Clin Microbiol Infect Dis* 6:633–634