

EDITORIAL

The diagnostic significance of relative bradycardia in infectious disease

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Relative bradycardia is an important diagnostic finding in a variety of infectious diseases. Relative bradycardia may be used to differentiate infectious diseases in selected clinical situations. Unfortunately, pulse-temperature differences have been vaguely described in a variety of publications and textbooks, leading to confusion on the part of clinicians in how to apply this information. Pulse-temperature relationships are based on physiological parameters, as is the calculation of a divergence of pulse and temperature recordings. Physiologically, for each degree increase in temperature in degrees Fahrenheit, there is a commensurate increase in the heart rate of 10 beats/min [1,2]. When temperature elevations are not accompanied by a physiologic increase in the pulse, the patient is said to have a pulse-temperature deficit. However, the term 'relative bradycardia' should only be applied to patients with temperatures in excess of 102 °F since the difference between pulse and temperature readings of ≤ 102 °F is insufficient to discern pulse-temperature abnormalities. The appropriate pulse for different degrees of temperature elevation is presented here in tabular form [2] (Table 1). Before one utilizes relative bradycardia as a diagnostic sign, the clinician should be sure to exclude other non-infectious conditions that result in pulse-temperature deficits. The most common cause of relative bradycardia or pulse-temperature deficits in patients with fever are β -blocker medications. β -Blockers decrease the pulse in patients with fever. Relative bradycardia as a diagnostic sign should not be applied in patients on β -blockers. However, digitalis derivatives, angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers do not affect pulse-temperature relationships as do β -blockers. A variety of non-infectious conditions also may present with relative bradycardia in febrile patients. These disorders are important to rule out for ascribing the pulse-temperature deficit to an infectious etiology. Central nervous system (CNS) disorders ranging from tumors to bleeds not infrequently are associated with relative bradycardia. Occasionally, lymphomas are associated with relative bradycardia. Lastly

and most importantly, drug fevers are regularly associated with relative bradycardia. Since drug fevers are the cause of approximately 10% of fevers in US hospitals, relative bradycardia is an important sign in the diagnosis of drug fever. Since many patients who are febrile have received, or are receiving, antimicrobials as well as other medications, a careful review of the patient's medications is necessary to be sure relative bradycardia is due to drug fevers and not an infectious cause [1-3].

Infectious diseases associated with relative bradycardia have important diagnostic significance for the individual patient as well as for the type of infection. Ostergaard and colleagues [4] from Denmark, in a well-performed study, confirmed that typhoid fever, Legionnaire's disease and psittacosis (*Chlamydia psittaci*) are associated with relative bradycardia. Equally as important, they confirmed that relative bradycardia is not a feature of *Mycoplasma pneumoniae* or other pulmonary infections due to typical bacterial pathogens. Relative bradycardia was not a feature of *Salmonella* non-enteric fevers, other Gram-negative infections, or viral infections. They concluded that relative bradycardia occurs only in diseases caused by Gram-negative intracellular pathogens [4]. A recent article by Wittsesjo and colleagues from Sweden studied sand fly fever and dengue fever as examples of viral diseases associated with relative bradycardia [5]. Both studies deserve notice because they are data-based and, more importantly, remind clinicians of the validity of relative bradycardia as an important clinical finding. I agree that relative bradycardia is a feature of these as well as other infectious diseases. Previously, I have stressed that the finding of relative bradycardia is one of the best ways to differentiate Legionnaire's disease from *Mycoplasma* in community-acquired pneumonias. Relative bradycardia is a constant feature with all species of *Legionella*, with a temperature > 102 °F [6,7].

In my experience, relative bradycardia is not limited to the Gram-negative intracellular organisms or selected viruses mentioned in the literature. Relative bradycardia is a feature of typhus and Rocky Mountain spotted fever, which are also intracellular Gram-negative organisms. Relative bradycardia is also a feature of leptospirosis, a Gram-negative but not intracellular organism. *Brucella* is an intracellular Gram-negative organism but is not associated with relative bradycardia. Furthermore, the protozoal parasites, malaria and babesiosis, are also regularly associated with relative bradycardia [1,8] (Table 2).

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Criteria	
Inclusive	
1. Patient must be an adult, i.e. ≥ 13 years.	
2. Temperature ≥ 102 °F.	
3. Pulse must be taken simultaneously with the temperature elevation.	
Exclusive	
1. Patient has NSR without arrhythmia, second/third-degree heart block or pacemaker-induced rhythm.	
2. Patient must not be on β -blocker medication.	
Appropriate temperature-pulse relationships	
Temperature	Beats/min
41.1 °f.f.s.C (106 °F)	150
40.6 °f.f.s.C (105 °F)	140
40.7 °f.f.s.C (104 °F)	130
39.4 °f.f.s.C (103 °F)	120
38.9 °f.f.s.C (102 °F)	120
38.3 °f.f.s.C (101 °F)	110

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Table 2 Causes of relative bradycardia

Infectious	Non-infectious
Legionella	β -blockers
Psittacosis	CNS lesions
Q fever	Lymphomas
Typhoid fever	Factitious fever
Typhus	Drug fever
Babesiosis	
Malaria	
Leptospirosis	
Yellow fever	
Dengue fever	
Viral hemorrhagic fevers	
Rocky Mountain spotted fever	

In summary, relative bradycardia is an important clinical finding if properly defined and applied. Non-infectious causes of relative bradycardia should be excluded before one can utilize this finding in the differential diagnosis of infectious diseases. Relative bradycardia is most useful in differentiating infectious diseases that resemble each other if a pulse temperature deficit is the discriminating variable, e.g. Legionnaire's disease versus *Mycoplasma* pneumonia, psittacosis or Q fever from tularemia pneumonia. Relative bradycardia is not helpful in differentiating malaria from typhoid

Table 1 Determination of relative bradycardia

fever or yellow fever from African hemorrhagic fevers, since all of these infections are regularly associated with relative bradycardia. As the clinicians' awareness of relative bradycardia increases, more studies will be done on different organisms to determine the pulse temperature relationships in known *Legionella* diseases as well as emerging infectious diseases, e.g. babesiosis. Relative bradycardia, properly defined and applied, remains an important clinical sign in the differential diagnosis of selected infectious diseases.

REFERENCES

- Cunha BA. The clinical significance of fever patterns. *Infect Dis Clin North Am* 1996; 10: 33–44.
- Cunha BA. Relative bradycardia as a diagnostic clue. *Intern Med* 1999; 20: 42–6.
- Cunha BA. Diagnostic significance of relative bradycardia. *Infect Dis Pract* 1997; 21: 38–40.
- Ostergaard L, Huniche B, Andersen PL. Relative bradycardia in infectious diseases. *J Infect* 1996; 33: 185–91.
- Wittesjo B, Bjornham A, Eitrem R. Relative bradycardia in infectious diseases. *J Infect* 2000; 38: 246–7.
- Cunha BA, Quintiliani R. The atypical pneumonias: a diagnostic and therapeutic approach. *Postgrad Med* 1979; 66: 95–102.
- Cunha BA. Clinical features of Legionnaire's disease. *Semin Respir Infect* 1998; 13: 116–27.
- Cunha BA. Bradycardia and lymphopenia in babesiosis. *Clin Infect Dis* 1998; 26: 1218–9.