

Clarifying misconceptions about Cope's sign

Ola *et al.*^[1] reported an unusual case of a young male with postprandial abdominal pain, recurrent syncope, and reversible complete heart block occurring during an episode of acute calculous cholecystitis, referred to as “Cope's sign” or cardio-biliary reflex. Another “Cope sign” eponymously named in honor of Sir Vincent Zachary Cope (1881–1974) refers to the bedside maneuver used in the diagnosis of acute appendicitis. Cope described in his book, *The Early Diagnosis of the Acute Abdomen* in 1921 the method for performing this sign:

It is well known that if there be an inflamed focus in relation to the psoas muscle the corresponding thigh is often flexed by the patient to relieve the pain. A lesser degree of such contraction (and irritation) can be determined often by making the patient lie on the opposite side and extending the thigh on the affected side to the full extent. Pain will be caused by the manoeuvre if the psoas be rigid from either reflex or direct irritation (p. 42).

O'Reilly and Krauthamer^[2] coined the term “Cope's sign” when they reported in the *British Medical Journal* two patients with cholecystitis and the physical finding of bradycardia, contrary to that previously experienced, described, and reported by Cope^[3] one year earlier in the same journal:

For six months before my recent illness, I occasionally had attacks of profuse sweating and increased pulse rate that woke me from sleep, but usually passed off within half an hour. They were not accompanied by any pain. A physician found my heart normal. (...) I do not know whether the nocturnal bouts of sweating and rise in pulse rate had any connexion with the presence of gallstones, but it may be of significance that since the operation a year ago I have not had a similar attack (p. 147-8).^[3]

What was particularly interesting is that during his last episode he experienced epigastric abdominal pain, a palpable distended gallbladder, and a normal pulse. Gallbladder distention, whether due to biliary colic or acute cholecystitis, may cause increased heart rate and arterial blood pressure and in animal models

decreased coronary blood flow secondary to reflex coronary vasoconstriction, findings consistent with activation of alpha-adrenergic sympathetic pathways.^[4] Cope's symptoms of recurrent episodes of increased pulse and diaphoresis occurring nocturnally were suggestive of biliary colic and chronic calculous cholecystitis with activation of sympathetic pathways.

The cardio-biliary reflex represents a group of disorders involving afferent and efferent neural pathways causing inappropriate vasodilation, bradycardia, hypotension, and syncope. The afferent signal originates in the gallbladder and is activated in response to mechanical stimulation causing vagally mediated bradyarrhythmia including atrioventricular block, which can be high grade or complete, along with other physical findings caused by *heightened* parasympathetic tone.^[5] What has been reported by Ola *et al.*^[1], O'Reilly and Krauthamer^[2], and other authors is a cardiac arrhythmia (bradycardia, heart blocks, and asystole) occurring in the setting of acute cholecystitis (cardio-biliary reflex) but not Cope's sign.

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There are no conflicts of interest.

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