Central sleep apnoea is a form of periodic breathing which resembles Cheyne-Stokes respiration but occurs only during sleep. One mechanism in the pathogenesis is a delay in chemical feedback from the lungs to the medullary respiratory centre. We explored the relationship between circulatory feedback delay in a patient with central sleep apnoea and Cheyne-Stokes respiration before and after mitral valve repair. Preoperatively the patient had severe central sleep apnoea and an increased circulation time. Following mitral valvuloplasty the circulation time was decreased with resolution of central sleep apnoea. This case demonstrates the role of feedback delay in central sleep apnoea and suggests that similar haemodynamic mechanisms may lead to central sleep apnoea and Cheyne-Stokes respiration.

Periodic breathing was first associated with severe heart failure by Stokes in the early 19th century. Subsequent investigators suggested that a delay in chemical feedback to the medullary respiratory centre was a major cause for the pattern of periodic breathing now known as Cheyne-Stokes respiration. Central sleep apnoea is characterised by respiration that starts and stops abruptly without significant variability in its frequency and depth, while Cheyne-Stokes respiration is characterised by a sinusoidal pattern in the frequency and depth of respiration. The mechanism of central sleep apnoea may be similar to that of Cheyne-Stokes respiration and be caused by a delay in chemical feedback to the medullary respiratory centre.

This case highlights the relationship between circulation time and central sleep apnoea. Our patient had central sleep apnoea in association with increased circulation time, both of which improved after mitral valvuloplasty. The patient’s mean (SD) arm to tongue circulation time was 50.9 (3.7) seconds which was much longer than the arm to tongue circulation time of 19.3 (1.9) seconds measured in two healthy subjects.

After mitral valvuloplasty the patient noted marked improvement in his sleep, daytime hypersomnolence, dyspnoea and fatigue, and a weight gain of 10 kg. An echocardiogram showed normal mitral valve motion and a low normal left ventricular ejection fraction (45–50%). The cardiac index by thermodilution improved from 1.4 l/min/m² immediately before the operation to 2.4 l/min/m² immediately afterwards. The mean (SD) arm to tongue circulation time decreased to 29.2 (1.7) seconds. Two months after the operation a sleep study showed complete resolution of the previously documented sleep apnoea (table 1).

DISCUSSION

This case highlights the relationship between circulation time and central sleep apnoea. Our patient had central sleep apnoea in association with increased circulation time, both of which improved after mitral valvuloplasty. The patient’s response suggests that circulation time plays a major role in the pathogenesis of central sleep apnoea.

In biological systems, periodic breathing may be produced by either altered chemosensitivity of the respiratory centre (controller gain), decreased oxygen stores, or by delayed chemical feedback (CO₂ and O₂) from the blood in the lungs to the respiratory centres in the central nervous system (feedback delay). The circulation time is a function of both cardiac output and blood volume: circulation time = blood volume/cardiac output. With the development of mitral regurgitation in our patient, a prolonged circulation time could have been caused by both increased blood volume from atrial enlargement and reduced forward cardiac output.

Previous studies have linked periodic breathing (Cheyne-Stokes respiration) with increased circulation time in
patients with congestive heart failure. In fact, clinical data have indicated similar prolongation of circulation time (30–54 seconds) in patients with congestive heart failure and Cheyne-Stokes respiration to that observed in our patient preoperatively. Periodic breathing can be induced by lengthening the circulation time in animals. In patients with congestive heart failure and Cheyne-Stokes respiration, cycle lengths were observed that were twice the lung to brain circulation time. Our patient had a similar 2:1 ratio with a cycle length of 70 seconds and a lung to artery circulation time of approximately 36 seconds (estimating a vein to lung time of 15 seconds in severe congestive heart failure from the data of Pryor and of Lange and Hecht). Following correction of our patient’s severe mitral regurgitation, the circulation time decreased markedly and periodic breathing during sleep resolved completely.

In addition to feedback delay, periodic breathing may also be caused by altered respiratory centre chemosensitivity (controller gain). For a given circulation time, an increase in the chemosensitivity of the respiratory control centres results in an increase in the tendency for breathing to oscillate. Although we did not measure oxygen chemosensitivity, previous studies have shown that supplemental oxygen decreases central sleep apnoea by decreasing the controller gain of the respiratory centre. Our finding that the apnoea/hypopnoea index decreased markedly on oxygen is consistent with the notion that a concomitant increase in controller gain also has a role in the pathogenesis of periodic breathing. Nevertheless, improvement in hypoxia while the circulation time remained prolonged did not eliminate sleep apnoea, which suggests that a prolonged circulation time played a major role in the pathogenesis of sleep apnoea in our patient.

This case report demonstrates the elimination of central sleep apnoea by a reduction in circulation time from markedly prolonged levels to near normal levels following surgical correction of severe mitral regurgitation. It highlights the similarity between the mechanism of central sleep apnoea and that of Cheyne-Stokes respiration. Our findings suggest that central sleep apnoea may be responsible for the sleep complaints in patients with congestive heart failure, including paroxysmal nocturnal dyspnoea.

**Authors’ affiliations**

A E Rubin, A R Schwartz, P L Smith, Department of Medicine, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

S H Gottlieb, Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

A R Gold, Division of Pulmonary · Critical Care Medicine, DVA Medical Center, Northpoint, NY and SUNY at Stony Brook School of Medicine, USA

Correspondence to: Dr P L Smith, Room 4B67, Johns Hopkins Asthma and Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD 21224, USA; plsmith@jhmi.edu

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**REFERENCES**

1 Stokes W. Diseases of the heart and aorta. Dublin: Hodges and Smith, 1854:324-5.
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