

15. Cochran W. The combination of estimates from different experiments. *Biometrics* 1954;**10**:101–129.
16. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539–1558.
17. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557–560.
18. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;**50**:1088–1101.
19. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–634.
20. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;**97**:1837–1847.
21. Mostofsky E, Maclure M, Sherwood JB, Tofler GH, Muller JE, Mittleman MA. Risk of acute myocardial infarction after the death of a significant person in one's life: the Determinants of Myocardial Infarction Onset Study. *Circulation* 2012;**125**:491–496.
22. Mittleman MA, Maclure M, Robins JM. Control sampling strategies for case-crossover studies: an assessment of relative efficiency. *Am J Epidemiol* 1995;**142**:91–98.
23. Mostofsky E, Burger MR, Schlaug G, Mukamal KJ, Rosamond WD, Mittleman MA. Alcohol and acute ischemic stroke onset: the stroke onset study. *Stroke* 2010;**41**:1845–1849.
24. Culic V, Eterovic D, Miric D, Rumboldt Z, Hozo I. Gender differences in triggering of acute myocardial infarction. *Am J Cardiol* 2000;**85**:753–756, A758.
25. Burg MM, Lampert R, Joska T, Batsford WV, Jain D. Psychological traits and emotion-triggering of ICD shock-terminated arrhythmias. *Psychosom Med* 2004;**66**:898–902.
26. Muller JE, Tofler GH, Stone PH, Muller JE, Tofler GH, Stone PH. Circadian variation and triggers of onset of acute cardiovascular disease. *Circulation* 1989;**79**:733–743.
27. Steptoe A, Kivimaki M. Stress and cardiovascular disease. *Nat Rev Cardiol* 2012;**9**:360–370.
28. Egger M, Schneider M, Davey Smith G. Spurious precision? Meta-analysis of observational studies. *BMJ* 1998;**316**:140–144.
29. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991;**133**:144–153.
30. Suls J. Anger and the heart: perspectives on cardiac risk, mechanisms and interventions. *Prog Cardiovasc Dis* 2013;**55**:538–547.

CARDIOVASCULAR FLASHLIGHT

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Differential clubbing and cyanosis: a pathognomonic finding in cardiology

Federico Moccetti, Beat A. Kaufmann, and Daniel Tobler*

Division of Cardiology, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland

* Corresponding author. Tel: +41 615565840, Fax: +41 612654598, Email: daniel.tobler@usb.ch

A 52-year-old woman was seen at the outpatient clinic for adults with congenital heart disease. Cardiac auscultation revealed a single and loud S2 and a soft pansystolic murmur of tricuspid regurgitation. On clinical examination, clubbing of the toes was noted and cyanosis was present only in the lower half of the body, whereas her fingers did not present evidence of clubbing or cyanosis (Panel A). Using the same pulse oximeter model simultaneously at her fingers and her toes while breathing room air, differential cyanosis (SO_2 toes 80%, SO_2 fingers 95%) could be confirmed (Panel B). On 10 L O_2 via nasal cannula SO_2 on the lower extremities remained unchanged, whereas SO_2 increased in the upper extremities. Echocardiographically, a suprasystemic right ventricular systolic pressure was measured (estimated systolic pulmonary arterial pressure 120 mmHg) with an arm-cuff blood pressure measurement of 115/83 mmHg (Panel C). As clinically suspected, a large patent ductus arteriosus (PDA) was found (marked with asterisk in Panel D).

The clinical finding of differential cyanosis as outlined above is pathognomonic for a large untreated PDA associated with Eisenmenger syndrome (shunt reversal into a right-to-left shunt due to progressive pulmonary vascular disease). The right-to-left shunt occurs just distal to the origin of the left subclavian artery, and central cyanosis is not evident in the upper part of the body. The continuous murmur of a large PDA is usually absent as balanced pressure in the systemic and pulmonic circulation is present (making it often difficult to depict flow by colour Doppler).

