

diagnostic testing broadens, there is a temptation to de-emphasise history and physical findings, and defer to the objective rigour of technology. Clearly, diagnostic test interpretation is not always straightforward. Making the picture even more complex, a significant barrier to routine use of probability-based test interpretation is the uncertainty inherent in pretest probability estimation, which includes the principles of the Bayes theorem.<sup>4</sup>

Indeed, on this complex background, I hope the central message in my article on ROC analysis was not lost in translation. Indeed, ROC curves help identify the most appropriate classification rules for test variables with a continuous outcome. ROC curves avoid confounding resulting from varying thresholds with subjective ratings. Finally, the ROC curve results should always be put into perspective, because a good classifier does not guarantee the eventual clinical outcome.

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**Competing interests:** None.

**Provenance and peer review:** Commissioned; not externally peer reviewed.

Accepted 1 July 2009

*J Clin Pathol* 2009;**62**:1051–1052.  
doi:10.1136/jcp.2009.069757

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## Revised national guidelines for the analysis of cerebrospinal fluid for bilirubin in suspected subarachnoid haemorrhage: interpret with caution

We wish to add a cautionary note regarding removal of the correction for serum bilirubin in the presence of increased cerebrospinal

fluid (CSF) bilirubin and oxyhaemoglobin from the revised national guidelines for the analysis of CSF for bilirubin in suspected subarachnoid haemorrhage (SAH).<sup>1</sup>

Recently we received a CSF sample requesting “xanthochromia” from a patient who had a normal CT brain scan. On CSF spectroscopy, both oxyhaemoglobin and bilirubin peaks were clearly visible. The net oxyhaemoglobin (OxyHb) and bilirubin absorbance were 0.0205 AU and 0.0146 AU, respectively. Under the revised guidelines<sup>1</sup> this would have been unequivocally but erroneously reported as “Bilirubin and oxyhaemoglobin increased. Consistent with subarachnoid haemorrhage.” Our laboratory policy, however, is that CSF bilirubin is always corrected for serum bilirubin irrespective of the presence or absence of OxyHb in patients with hyperbilirubinaemia. The patient’s serum bilirubin was 60 µmol/l, correction for which<sup>2</sup> wholly accounted for the increased net bilirubin absorbance.

The patient, on discussion with the medical team, had chronic alcoholic liver disease and presented with headache and confusion. A “difficult” lumbar puncture was undertaken primarily but not exclusively to exclude tuberculous meningitis. An otherwise normal CSF led to a diagnosis of hepatic encephalopathy. We explained the CSF spectroscopy findings to be due to a combination of a traumatic lumbar puncture and hyperbilirubinaemia. It is worth noting that a similar picture of CSF OxyHb and bilirubin, in the absence of SAH and hyperbilirubinaemia, may also be the result of repeated attempts at lumbar puncture, and these too would erroneously be reported as “Bilirubin and oxyhaemoglobin increased. Consistent with subarachnoid haemorrhage” under the revised guidelines.<sup>1</sup>

We therefore suggest that:

- ▶ Increased CSF bilirubin is always adjusted for hyperbilirubinaemia and not just in the absence of visible oxyhaemoglobin peak as recommended,<sup>1</sup> to avoid misdiagnosis and clinical misdirection. This is especially important because: firstly, the combination of increased CSF bilirubin and OxyHb in the presence of hyperbilirubinaemia is rare,<sup>3,4</sup> and it is therefore likely to be overlooked; and secondly, traumatic lumbar punctures are common.<sup>4</sup> These findings, therefore, would not be uncommon on spectroscopic scanning of CSF samples from jaundiced patients.
- ▶ The use of computer programs and algorithms based guidelines to interpret CSF spectroscopy may lead to erroneous diagnosis if the clinical information and laboratory investigations are not considered together when reporting CSF spectroscopy findings. In our department, therefore, all scans are reviewed by a senior member of staff.

#### Interactive multiple choice questions

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**Competing interests:** None.

**Provenance and peer review:** Not commissioned; not externally peer reviewed.

Accepted 7 August 2009

*J Clin Pathol* 2009;**62**:1052. doi:10.1136/jcp.2009.069732

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## To study the effect of the sequence of seven pranayama by Swami Ramdev on gene expression in leukaemia patients and rapid interpretation of gene expression

Deep breathing at six breaths per minute has been recently reported to be associated with a significant reduction in the frequency of

premature ventricular complexes.<sup>1</sup> Oxidative stress may contribute to the pathophysiology of many chronic diseases.<sup>2</sup> Regular practice of pranayama balances between the concentration of reactive oxygen species and physiological antioxidants and maintaining better antioxidant status.<sup>3</sup> The aim of the present study is to record the effect of the pranayama on the human genome in the practitioners and non-practitioners of Swami Ramdev Yog in patients with chronic lymphocytic leukaemia. Each year, 3000 to 4000 new cases of chronic lymphocytic leukaemia (CLL) are diagnosed in the UK. Many genes involved in stress signalling molecules are found to be activated under conditions of modified breath in specific posture. Yog can play a useful role in patients with cancer. This experiment was designed to study gene-expression profiling for eight patients with RNA samples from whole blood using two replicates for each sample. In this study, we report on the profiling of ~28 000 human genes before and after the Swami Ramdev Yog sequence in patients with leukaemia cancer by using the Expression Array System of Applied Biosystems (Foster City, California). Fifteen millilitres of blood was collected by venipuncture, in EDTA-containing tubes, from the study subjects as well as controls after informed consent. Total RNA samples obtained from the blood of all eight patients were processed into labelled cRNA using the Applied Biosystem Chemiluminescent RT-IVT labelling kit.

The practitioners included subjects in the age range of 18–55 years males and from the same socio-economic status, had comparable body weights (+10%), and were vegetarians and non-smokers. The fold change of control versus intervention group sample was analysed by filtering the dataset using p values <0.01 and a signal-to-noise ratio >3 for use in the ANOVA statistical analysis. Of these ~28 000 genes, 69 genes were upregulated up to 16-fold, and 4428 genes were upregulated up to twofold in practitioners of seven sequences of Swami Ramdev Yog. We use the Spot fire software for the determination of fold changes for the differentially expressed genes. There was a significant increase in expression of AK, BC, NM BX, R-26 and hCG ( $p = 0.034$ ) in practitioners of seven sequences of Swami Ramdev Yog as compared with the normal controls. This study is the first of its kind which reflects the significant effect on stress-related signalling pathways in the human body by the practice of pranayama. The observed upregulation of AK, BC, NM BX, R-26, hCG in Swami Ramdev Yog practitioners perhaps suggests a prolonged life span of WBCs by inhibition of apoptosis. Upregulation of antiapoptotic Bcl-2 along with Cox-2 gene expression in lymphocytes of Swami Ramdev Yog group also suggests a better immune regulation by prolonging the life-span of lymphocytes in the practitioners.

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**Acknowledgements:** This study was inspired by Yog Guru Swami Ramdev and my beloved wife, Abhilasha. This work was carried out in collaboration with Applied Biosystems.

**Competing interests:** None.

**Ethics approval:** Ethics approval was provided by IEC of Patanjali Yogpeeth.

**Patient consent:** Obtained.

**Provenance and peer review:** Not commissioned; not externally peer reviewed.

Accepted 20 July 2009

*J Clin Pathol* 2009;**62**:1052–1053.  
doi:10.1136/jcp.2008.061580

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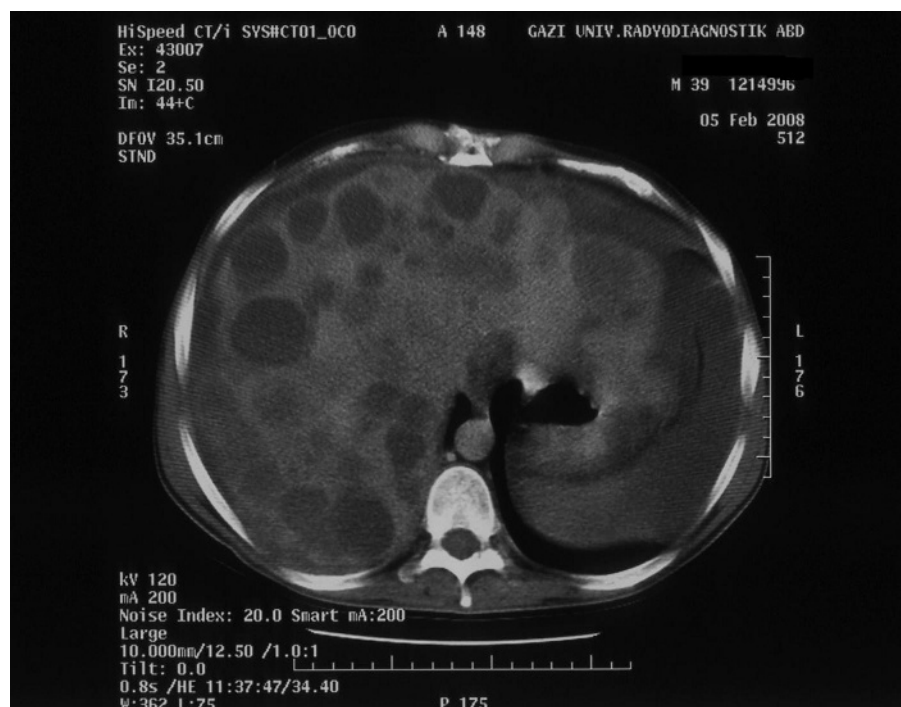
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### CORRESPONDENCE

## Adult hepatic epithelioid haemangioendothelioma presenting with Kasabach–Merritt syndrome: a case report

Kasabach-Merritt syndrome (KMS) is a serious consumptive coagulopathy with thrombocytopenia, associated with benign or malignant vascular tumours or malformations. Although it is generally reported with childhood vascular tumours, there is limited data about adult vascular tumours associated with KMS. Hepatic epithelioid haemangioendothelioma (HEHE) is a rare vascular neoplasm of the liver with intermediate malignant potential. In adult patients, HEHE associated KMS has reported in several case reports. A 39-year-old male patient with epithelioid haemangioendothelioma in the liver and KMS is described here. He presented with multiple bilobar liver metastasis and severe thrombocytopenia, anaemia and coagulopathy. Immunohistochemistry showed diffuse cytoplasmic staining with CD34 and vimentin; thus the diagnosis of epithelioid haemangioendothelioma was confirmed. It is believed that this patient is the third case with adult HEHE associated with KMS reported in the literature.

Hepatic epithelioid haemangioendothelioma (HEHE) is a rare vascular neoplasm of the liver with low malignant potential.<sup>1</sup>



**Figure 1** Multifocal and bilobar appearance of haemangioendothelioma at axial contrast enhanced CT scan of the liver.



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*J Clin Pathol* 2009 62: 1052-1053  
doi: 10.1136/jcp.2008.061580

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