Use of CT-PET imaging in investigation of pyrexia of unknown origin

Sir,

Pyrexia of unknown origin continues to intrigue and elude clinicians, providing challenging clinical conundrums (Knockaert et al, 2003; Varghese et al, 2010). The use of computed tomography-positron emission tomography (CT-PET) imaging in pyrexia of unknown origin is not well established (de Kleijn et al, 1997). Published case series suggest it has very low diagnostic yield in patients without raised inflammatory markers (Bleeker-Rovers et al, 2009; Varghese et al, 2010).

The authors retrospectively reviewed the contribution of CT-PET scans to diagnosis of pyrexia of unknown origin at the Hospital for Tropical Diseases, London, from 2005–10. Thirty-three HIV negative patients (mean age 56 years, 21 male) had CT-PET imaging; 19 were inpatients and 14 were outpatients. Thirty patients (91%) had had previous imaging during investigation of pyrexia of unknown origin, including cross-sectional CT in 18 (54%). Final diagnoses were two cases of malignancy, nine which had an inflammatory or autoimmune basis, eight were infection, five were 'other', and nine were inconclusive (three patients died during evaluation). *Table 1* details the role of CT-PET in diagnostic evaluation.

The data involved a heterogeneous group, requiring a systematic exhaustion of tests, and these patients were often managed over long time periods with trials of therapies. CT-PET seemed to have been used as a last resort when conventional imaging was inconclusive and the clinician was debating the use of invasive tests. In this setting, a tertiary care centre in an inner-city location, CT-PET contributed minimally to diagnosis of pyrexia of unknown origin. Although 73% had an abnormal CT-PET, in only one patient (8%) did the new findings actually provide a diagnosis, and CT-PET made no contribution to diagnosis in patients with normal inflammatory markers. While it could be argued that CT-PET had use as a rule-out investigation, in the absence of any noted benefit and with significant cost, this should be interpreted cautiously.

The strength of these data is that they were based on detailed, chronological, case-record-based analysis of the contribution of CT-PET scanning to diagnosis. Undeniably, it was a small sample, and causes of pyrexia of unknown origin for which CT-PET has particularly high diagnostic yield over other cross-sectional imaging, e.g. large vessel vasculitis, were not represented in this group. Patients with pyrexia of unknown origin are a variable case-mix, and this may affect the investigations required. There is also disparity in access to CT-PET. In a tertiary centre, such as ours, patients with pyrexia of unknown origin have already been subject to extensive imaging. Further, there are limitations in making assessment based on a retrospective review. In this audit, the indications for CT-PET were determined from scan request forms as well as documentation in the notes. Similarly, conclusions made by the team and investigations that followed were dependent on this documentation.

These results and review of the literature emphasize the need for larger, prospective studies of the use of CT-PET in pyrexia of unknown origin, and sub-groups for which it has a particular role. These should objectively assess clinically relevant contributions to better inform diagnostic algorithms.

On reflection, a multidisciplinary approach (including infection specialists and nuclear medicine specialists) should improve decision making regarding the role of CT-PET in individual patients. There is a clear role in patients with contraindications to contrast. It has a very low yield in patients with normal inflammatory markers (Knockaert et al, 2003; Varghese et al, 2010). While current guidelines recommend CT-PET late in the diagnostic pathway, as followed in the authors' practice, prospective studies should explore the role of CT-PET as a first-line investigation in distinct pyrexia of unknown origin syndromes (Royal College of Radiologists, 2010; Varghese et al, 2010).

Table 1. Key findings

Patients (number)	Abnormal CT-PET No. (%)	Nodal uptake No. (%)	Other uptake No. (%)	Invasive investigations No. (%)	New findings from CT-PET (not identified on previous imaging) No. (%)	New finding deemed to be the cause of the PUO No. (%)
All patients (33)	24 (73)	15 (46)	15 (46)	14 (42)	13 (39)	1 (8)
Raised inflammatory markers (24)	20 (83)	12 (50)	11 (46)	12 (50)	11 (46)	1 (9)
Normal inflammatory markers (9)	4 (45)	3 (33)	4 (44)	2 (22)	3 (33)	0 (0)

CT-PET = computed tomography-positron emission tomography; PUO = pyrexia of unknown origin

Tehmina Bharucha/Mike Brown
Core Medical Trainee/Infectious Diseases Consultant
Hospital of Tropical Diseases
University College London Hospital
London WC1E 6JD
(t.bharucha@doctors.org.uk)

Bleeker-Rovers CP, van der Meer JW, Oyen WJ (2009) Fever of unknown origin. *Semin Nucl Med* **39**: 81–7
de Kleijn EM, Vandenbroucke JP, van der Meer JW (1997) Fever of unknown origin (FUO): a prospective multicenter study of 167 patients with FUO, using fixed epidemiologic entry criteria. The Netherlands FUO Study Group. *Medicine (Baltimore)* **76**: 392
Knockaert DC, Vanderschueren S, Blockmans D (2003) Fever of unknown origin in adults: 40 years on. *J Intern Med* **253**: 263–75
Royal College of Radiologists (2010) *Indications for PET-CT: guidance from The Royal College of Radiologists.* Royal College of Radiologists, London
Varghese G, Trowbridge P, Doherty T (2010) Investigating and managing pyrexia of unknown origin in adults. *BMJ* **341**: c5470

Sleep-induced hypoxaemia: remember medroxyprogesterone and acetazolamide

Sir,

The article by Zhang et al on sleep-related hypoxaemia in chronic obstructive pulmonary disease (COPD) (vol 74(9), 2013, p. 497) discusses some more commonly used pharmacological treatments for hypoxaemia. However, another three drugs have been studied in the context of sleep-related hypoventilation and are worth mentioning.