and required mechanical ventilation for 14 days. Serum triglyceride concentration on the day of admission was high (3·4 mmol/L).

Serum concentrations of aminoacids and organic acids were normal. Because of her arthrogryposis, a muscle biopsy was done, which showed decreased complex IV activity, cytochrome oxidase ratio 0·004 (reference range 0·014–0·034), and suggested possible mitochondrial respiratory-chain enzyme deficiency. These results were interpreted with caution because the sample had a high fat content. Urine was negative for myoglobin, and microbiological and virological tests were negative.

The child's clinical features (lactic acidosis, myocardial failure, renal failure, and hypertriglyceridaemia) are consistent with propofol infusion syndrome.[2] However, our report like previous reports shows little evidence to prove a direct link between propofol and multisystem illness. Cray and colleagues[3] reported a similar idiosyncratic multisystem reaction to propofol and detected an unknown compound in the child's blood, which they presumed to be a metabolite of propofol. Furthermore, sepsis, malignant hyperthermia, and hypoxia may have contributed. The presence of arthrogryposis in our case suggests an underlying neuromuscular defect, although results of tests on muscle were inconclusive. Cray and colleagues also described a mitochondrial respiratory-chain defect but suggested that it was a possible mechanism of damage caused by propofol rather than an underlying neuromuscular defect. Genetic predisposition in certain children may render them susceptible to an often fatal idiosyncratic reaction in response to propofol infusion. Complete recovery after supportive care also suggests a toxin-mediated illness in our patient.

Although there are reports on the safe use of propofol in children, the adverse reactions to propofol cannot be ignored. As is the case with so many other non-licensed drugs in paediatric practice, propofol infusions in children need to be the subject of a controlled trial.

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Acute coronary syndromes

Sir—The unresolved debate about primary-invasive approach versus primary-medical approach in patients who present with an acute coronary syndrome is clearly shown by the opposing statements in *The Lancet*'s June supplement on this challenging topic. Freek Verheught (June 12, suppl II, p 16)[1] states that: "This applies both to the high-risk patients, in whom a routine invasive strategy of this approach may be harmful (for example, in VANQWISH)". By contrast, if Joseph Delehanty and colleagues (June 12, p 24)[2] had an acute coronary syndrome, they would favour an invasive strategy: "Individuals at high risk of myocardial infarction or death should undergo an early invasive intervention". If I had an acute coronary syndrome, I would hopefully have the opportunity to decide on the unanimous results of trials that compare these different approaches.

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Sir—In the well-crafted review and update on the diagnosis of acute coronary syndromes by Peter Klootwijk and Christian Hamm (p 10)[1] I found an unexpected phrase that I cannot let pass without retort. They point out that physicians can now use rapid testing systems for troponins at the bedside and generate test results within 15–20 min. I disagree with their indication that point-of-care testing in a hospital setting is typically done "independent of a clinical chemistry facility".

Whether at a bedside, an emergency room, or in a laboratory, I expect that qualitative or quantitative biochemical tests used to support medical decisions should be assessed and implemented with the cooperation and guidance of laboratory staff. The laws and regulations surrounding the legal need to involve the clinical laboratory in bedside testing vary in different countries and locales. Consultation of laboratory physicians and clinical scientists is particularly relevant for the implementation of cardiac troponin-I testing and the establishment of interpretation thresholds, because of variation between manufacturers that generates from two-fold to more than 20-fold differences in concentration.[2] As a consequence of this variation the value of troponin tests shown in clinical trials is mostly manufacturer-specific. Qualitative tests are not exempt from standardisation issues, because they are designed to indicate positive or negative results at a concentration threshold that is prone to this variability.

I sympathise with the investigators because these analytical issues are difficult to convey when reviewing the outcomes of clinical trials. I expect that through the efforts of the International Federation of Clinical Chemistry and Laboratory Medicine and other national organisations that cardiac-marker testing will soon have internationally accepted standards and I hope the co-dependent relationship between the laboratory and the ward staff will continue to be mutually recognised.

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Lipodystrophy in HIV-1-infected patients

Sir—Andrew Carr and colleagues (June 19, p 2093)[1] report the results of a longitudinal study of 113 HIV-1-infected patients who were receiving protease inhibitors and were followed up for 21 months (92 cases of lipodystrophy) and 45 treatment-naïve patients who were followed up for 28 months (one case of lipodystrophy). They propose a classification of lipodystrophy associating the clinical anomalies with metabolic disorders that would make the results of different studies sufficiently homogeneous for comparisons to be made. Comparison between patients with and without lipodystrophy showed that the former had taken protease inhibitors and had been HIV-1-seropositive for longer, but that their CD4-cell counts and virus loads were similar. Development of lipodystrophy did not seem to be associated with the particular protease inhibitor used, but onset was more rapid with ritonavir or saquinavir.

Some of our findings corroborate those of Carr and colleagues. We used the same clinical (with patients self-reporting) and biological selection criteria, and diagnosed 61 (26·2%) lipodystrophy cases among our 233

	Without lipodystrophy		With lipodystrophy		p*
	Patients	Mean (SD) duration (months)	Patients	Mean (SD) duration (months)	
Nucleoside analogues					
Zidovudine	106	23·9 (20·0)	45	29·7 (22·1)	0·11
Didanosine	72	13·9 (11·9)	26	15·5 (15·9)	0·60
Zalcitabine	67	20·0 (12·2)	39	16·2 (8·9)	0·08
Lamivudine	107	15·3 (6·3)	47	17·9 (6·7)	0·02
Stavudine	98	15·4 (8·2)	49	18·2 (7·7)	0·04
Protease inhibitors					
Saquinavir	52	12·9 (7·4)	31	13·5 (7·3)	0·72
Ritonavir	19	9·5 (8·9)	13	12·6 (6·1)	0·29
Indinavir	51	12·3 (9·0)	39	13·7 (8·6)	0·52
Nelfinavir	49	4·2 (3·0)	27	5·0 (2·9)	0·26

*For difference in duration.

Duration of exposure to antiretroviral drugs

HIV-1-infected patients: two (3%) had not been treated, five (8%) had received a two-drug regimen, and 54 (89%) were taking at least three drugs, one of which was a protease inhibitor. Compared with patients without lipodystrophy, patients with lipodystrophy were older (38·8 [SD 9] *vs* 44·8 [10·2] years, p<0·0001), had lower mean CD4-cell counts (503 [270] *vs* 395 [259]/μL; p=0·007), and a greater proportion had progressed to AIDS (17·1 *vs* 38·3%, p=0·0007; odds ratio 3·2 [95% CI 1·47–6·2]); the mean body-mass index differed only slightly (22·8 [3·10] *vs* 21·9 [2·54] kg/m^2, p=0·03), and virus loads were similar (72·7 *vs* 67·2% with <500 copies/mL).

Among 216 (92·7%) patients on therapy, 140 (64·8%) were receiving a protease inhibitor. Among the 59 patients with lipodystrophy who were being treated, 46 (78%) were receiving a protease inhibitor. At the time of lipodystrophy diagnosis, lamivudine was being taken by 160 (74%) and stavudine by 147 (68%) treated patients, compared with 45 (76%) and 46 (78%), respectively, of those with lipodystrophy. We calculated the theoretical duration of exposure to antiretroviral drugs of all our patients since the first day of treatment and found no difference between patients with and without lipodystrophy (table). We believe that the significant association with lamivudine and stavudine (p<0·05) may be biased because of the large number of patients treated with these drugs who had previously received other nucleoside analogues. However, all patients with lipodystrophy had been treated longer than patients without this disorder.

At present, no drugs can be associated more than another with the development of lipodystrophy. Intensification of therapy with a protease inhibitor increases the risk of lipodystrophy as a function of age, CD4-cell count, and disease stage (ie, patients treated for longer with multiple antiviral agents).

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1 Carr A, Samaras K, Thorisdottir A, Kaufmann GR, Chisholm DJ, Cooper DA. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet* 1999; **353:** 2093–99.

Sir—Andrew Carr and colleagues[1] report a 74% prevalence of lipid abnormalities in HIV-1-infected patients who had been on protease inhibitors for a median of 21 months. We evaluated a cohort of 159 HIV-1-infected patients on protease-inhibitor therapy in a cross-sectional study to assess the prevalence of metabolic abnormalities. Cut-off values for hypercholesterolaemia, hypertriglyceridaemia, normal HDL cholesterol, and LDL cholesterol are defined elsewhere.[1,2]

We assessed 120 men (75·5%) and 39 women (24·5%) with a median duration of HIV-1 infection of 63 months. 57 (35·8%) patients had been injecting drug users. All patients had been receiving highly active antiretroviral therapy (HAART) including at least one protease inhibitor therapy. 104 (66·7%) had undetectable plasma viral load at the time of the study. 62 (39·2%) patients met the criteria for lipodystrophy.[1] 110 (69·2%) patients did not undertake regular physical activity, 102 (64·1%) were smokers, 29 (18·2%) consumed more than 20 g alcohol daily, and six (3·8%) had a history of hypertension. Body-mass index was above the upper normal limit in 53 (33·3%) patients and the waist/hip ratio (normal upper limit 0·95 in men and 0·85 in women) was increased in 83 (52·2%) patients. Hypertriglyceridaemia was detected in 72 (45·3%) patients, hypercholesterolaemia in 58 (36·5%), low HDL-cholesterol concentrations in 68 (44·2%), and high LDL-cholesterol concentrations in 52 (32·9%). Overall, lipid variables were normal in only 44 (27·7%) patients. Nine (5·7%) patients had diabetes mellitus.

Our results agree with those of Carr and colleagues in that roughly 25% of our HIV-1-infected patients receiving treatment with protease inhibitors had normal serum lipid profiles after 1 year of treatment, only 6% had diabetes, and more than 50% had central adiposity. HAART has had a striking impact on the natural course of HIV-1 infection, increasing the life expectancy of HIV-1-infected patients.[3,4] However, the central adiposity and lipoprotein profile associated with protease inhibitors is in turn associated with substantial cardiovascular morbidity.[5] A high prevalence of diabetes mellitus was seen which exceeded that expected for the general population of similar age. These risk factors combined with the high prevalence of physical inactivity and smoking makes long-term treatment with HAART worrisome.

Screening for hyperlipidaemia and abnormalities of glucose homoeostasis in patients receiving HAART and correction of other risk factors is essential. Lifestyle modification and pharmacological therapy are needed to achieve control of the clustering of cardiovascular factors associated with HAART to prevent excess vascular disease morbidity and mortality among HIV-1-infected patients.

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