therapy (LTOT) is important, especially as, 
anecdotaly, some clinicians seem to con-
sider LTOT to be an absolute contraindica-
tion to intubation. Table 1 summarises the 
outcomes for intubated patients with 
chronic obstructive pulmonary disease 
(COPD) in the COPD and Asthma 
Outcome Study (CAOS), comparing those 
who were on LTOT before admission with 
those who were not. It can be seen that, 
although the two groups of patients had 
similar 180-day survival rates, the LTOT 
group had significantly lower EuroQol 
scores. These differences partly reflect differ-
ences in health status before the onset of the 
acute episode (at that stage 63% of the 
LTOT group were housebound, chairbound 
or bedbound compared with 27% of the rest) 
and partly the higher proportion of the 
LTOT group who felt that their health at 
180 days was worse than it had been before 
onset. Nevertheless, in our data, 86% would 
choose ICU and intubation again. The 
actual number of patients on LTOT who 
responded to the follow-up questionnaire 
was small and the confidence interval wide 
(58–98%). It is also possible that the small 
numbers of patients with COPD on LTOT 
currently being admitted to critical care are 
aptically positive about invasive proce-
dures, at least in retrospect. Nonetheless, 
the straightforward interpretation of these 
data is that, from the perspective of the 
patient with COPD, intubation is not 
ful—even for those on LTOT. If so, 
patient preferences must often be frustrated 
by limits on the availability of ICU beds. 
What the threshold should be for intubation 
in terms of probability of survival and how 
patients’ (or carers’) perspectives might be 
brung into decisions on intubation are 
currently unanswered questions.

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Competing interests: None.

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

Accepted 25 June 2009


Iloprost-induced rash

We report a 59-year-old woman with a 
background history of CREST syndrome 
(calcinosis, Raynaud phenomenon, (o)eso-
ophageal dysmotility, sclerodactyly and tel-
angiectasia) and secondary pulmonary 
hypertension who presented with a bilateral 
lower limb vasculitic rash.

A couple of weeks earlier she had been 
initiated on nebulised iloprost (Ventavis; 
Bayer New Zealand, Auckland, New 
Zealand) for progression of her pulmonary 
hypertension while on treatment with 
Sildenafil. She started on 20 μg three times 
a day, increasing every 3 days to a total of 
20 μg every 4 h. Within a few days of 
reaching the maximum dose she developed 
a painful vasculitic rash over both lower 
limbs, which did not respond to analgesia 
and emollients (see fig 1). The dose of 
iloprost was reduced slowly over a couple 
of weeks to 15 μg three times a day. During 
this time, the rash improved considerably.

Unfortunately, she continued to deterio-
rate and was admitted to hospital pro-
doundly hypoxic. Oxygen therapy and 
diuretics were increased with minimal 
effect. The decision was made to re-chal-
lenge with an increased dose of iloprost, 
hoping that dual therapy with appropriate 
dosing may ameliorate her pulmonary 
hypertension.

After only two doses at 20 μg, the rash 
recurred dramatically and became intoler-
able. On reducing the iloprost dose to 15 μg, 
the rash again improved. She was discharged 
home with assistance from palliative care 
and died a week later.

Iloprost is a stable analogue of prostacy-
clin which is synthesised in the vascular 
endothelium, and it shows a pharmacologi-
cal profile similar to that of endogenous 
prostacyclin. Its vasodilating effects are used 
clinically to treat moderate to severe pul-
monary hypertension.

Various side effects of iloprost have been 
reported, including flushing, dizziness, 
cough, headache, spasm of the jaw muscles, 
back pain, vomiting and diarrhoea.

Bleeding events were common in clinical 
trials, especially in patients also taking anti-
ocagulants.2 Iloprost is known to interfere 
with platelet aggregation; however, this effect 
is more common and more pronounced with 
intravenous use.3 Of note, our patient did not 
develop thrombocytopenia.

Cutaneous drug reactions are common, 
with an incidence of 2–5% in hospital 
patients. Almost any drug can cause rash; 
most common are antibiotics and non-
steroidal anti-inflammatory drugs 
(NSAIDs). Drug-induced small vessel vascu-
latin (or hypersensitivity vasculitis) is rarer. 
This is generally limited to the skin, but can 
occur as an element of a systemic illness. 
The rash is purpuric, palpable and occurs in 
dependent areas. Biopsies show a cellular 
infiltrate of small vessels often with leuco-
cytoclastic. The most common causes are 
drugs and infection.4

Adverse drug reactions can be difficult to 
diagnose, and scoring systems may help.5 In 
our patient the vasculitic rash appeared after 
initiation of iloprost and improved when the 
dose was reduced. More importantly, it 
deteriorated with a repeat drug challenge. 
This gives a high probability of a drug 
reaction. In a different clinical scenario, 
cessation of the drug may well result in 
complete resolution of the rash.

To our knowledge, this is the first 
reported case of iloprost-induced vasculitic 
rash. The precise mechanism and frequency 
are unknown. Clinicians should be aware of 
this potential adverse effect, and the drug 
should be reduced or stopped if possible.

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Hepatotoxicity and antituberculosis therapy: time to revise UK guidance?

Hepatotoxicity associated with antituberculosis therapy is an important clinical problem. Guidelines recommend baseline liver function tests (LFTs) before commencing treatment. In patients with risk factors for hepatotoxicity (e.g., chronic viral hepatitis or liver disease, pregnancy or significant alcohol history) or abnormal baseline LFTs, further monitoring is indicated whilst on treatment.1,2 In all other cases repeat liver function testing is reserved for patients developing symptoms suggestive of liver dysfunction (fever, malaise, nausea, vomiting, abdominal pain, jaundice or unexplained fatigue). HIV co-infection is not specifically mentioned within UK guidance. Given increasing national rates of tuberculosis/HIV,3 we assessed how this might impact upon current guidelines.

A retrospective case-note review was undertaken of patients treated for active tuberculosis over a year (1 June 2006–31 May 2007) at our central London hospital. Hepatotoxicity was defined as elevation of alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than three times the upper limit of normal (>3ULN).

A total of 103 patients started antituberculosis treatment; 55 were male. The median age was 43 years, with two patients under the age of 16 (range 0–82 years). The population was ethnically diverse: 24 Asian, 46 Black African, 22 European, 11 other. Seventy-nine percent of patients were tested for hepatitis B (9% were positive), 77% for hepatitis C (9% were positive), 5% were pregnant, 5% had a significant alcohol history and 2% had other chronic liver diseases.

The minimum prevalence of HIV co-infection was 23%; 19 patients were known to be HIV positive at baseline. A further 60/84 (71%) had HIV tests; and five patients were new HIV diagnoses.

Seven patients (four of whom were HIV co-infected) with ALT/AST >3ULN at baseline and two patients with no LFTs performed were excluded from analysis. In the remaining 94 subjects, the incidence of hepatotoxicity was 15% (14/94). Of these 57% (8/14) had symptoms consistent with hepatotoxicity, indicating the need for LFT testing; however, 21% (3/14) were asymptomatic. For the remainder, data on symptoms were not clearly available. Ten percent (9/94) developed ALT/AST >3ULN (here, 67% of patients were symptomatic; 11% asymptomatic, 22% symptom data not available). The median time to first abnormal and highest ALT/AST was 6.5 days (range 2–18 days) and 29.5 days (range 7–176 days), respectively. There was a significant difference in hepatotoxicity between HIV-positive and HIV-negative populations: 7/20 (35%) vs 4/55 (7%), respectively (p = 0.006, Fisher’s exact test). Concurrent use of antiretroviral therapy did not increase the risk in the former (p = 0.11, Fisher’s exact test) (fig I).

In 51 patients with normal baseline LFTs and no risk factors for hepatotoxicity, the incidence of hepatotoxicity was 10% (5/51). When HIV-positive individuals were excluded, this fell to 2% (1/44). Furthermore, all three subjects who were asymptomatic at the time of their rise in ALT/AST were HIV co-infected.

In conclusion, most cases of hepatotoxicity continue to be identified by current guidelines, although HIV co-infection does appear to impact upon both the incidence of hepatotoxicity and the use of the recommended algorithm (where LFT monitoring on treatment is indicated according to symptoms). The 1998 British Thoracic Society guidance implies that testing for viral hepatitis should be undertaken at tuberculosis diagnosis.2 Our results suggest that routine HIV testing would identify patients not only requiring treatment for HIV but also at risk of hepatotoxicity. Although a small sample size, we believe our findings will be reproducible in other tuberculosis populations, and that this strengthens the argument for HIV testing to be offered universally in this setting; an approach which avoids “risk assessment” for HIV, which in itself can generate anxiety and stigma.5

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HIV, which in itself can generate anxiety and stigma.

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Competing interests: None.

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

Accepted 3 June 2009

Thorax 2009;64:918. doi:10.1136/thx.2009.115469

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Figure 1 Tuberculosis/HIV co-infected patients (with normal baseline liver function tests). Comparison of antiretroviral (ARV) use in hepatotoxic and non-hepatotoxic populations.