toxicity of the *C. difficile* toxins [10]. The release of interleukin-1 (IL-1) and tumour necrosis factor (TNF) from monocytes induced by these toxins may contribute to the bowel inflammation [11]. Recently, Vlasveld and associates [12] suggested that GM-CSF might be a cofactor in the pathogenesis of enterocolitis. Experimental data on *C. difficile* toxins A and B showed that they strongly induce release of TNF, IL-1 and IL-6 by monocytes [11]. The fact that rhu-GM-CSF itself induces TNF release from monocytes may have led them to their hypothesis [13]. Maximum TNF levels were observed 3–4 days after rhu-GM-CSF application in neutropenic patients [14]. Despite these theoretical drawbacks, the administration of rhu-GM-CSF was associated with prompt resolution of safe granulocyte counts and prompt recovery from enterocolitis in our patients.

Apparently, the positive effect of rapid restoration of a functionally active granulomonocytic defense system by far outweighs theoretical shortcomings of secondary cytokine release.

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Short-term Versus Continuous Infusion: No Influence on Ifosfamide Side-chain Metabolism

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IFOSFAMIDE (IFO) is a widely used anticancer drug which requires metabolic activation by hydroxylation of the ring system to exert cytotoxic activity. A second metabolic pathway produces the cytostatically inactive metabolites, 2-dechloroethylifosfamide (2-D-IFO) and 3-dechloroethylifosfamide (3-D-IFO), releasing chloro-acetaldehyde. This pathway of side-chain metabolism has been discussed as a source of CNS toxicity [1–3] and in connection with renal toxicity [4]. As regards neurotoxicity, the incidence seems to be strongly schedule-dependent [5]. However, antitumour efficacy was also lower in patients on a continuous IFO application schedule [6].

We, therefore, compared the urinary exception of IFO, 2-D-IFO and 3-D-IFO on short-term and continuous ifosfamide infusion (3g/m²/daily). In 13 children, of whom 6 received IFO by 1 h infusion and 7 by continuous infusion, urine output up to 72 h was completely sampled and investigated by gas chromatography (Figure 1).

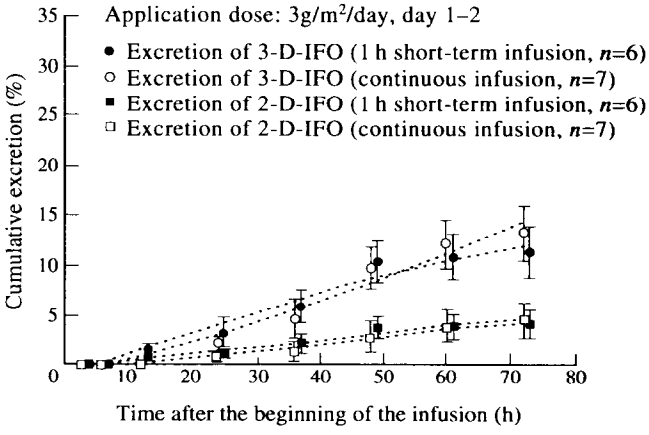

Figure 1. Cumulative excretion of side-chain metabolites (in % of the totally applied dose).

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Overall, neither the excretion kinetics (Figure 1) nor the total amount of side-chain metabolites formed showed relevant schedule dependency. Even with a 1-h infusion, there was a lag of 3–6 h until dechloroethylation became relevant. The excretion pattern of unmetabolised IFO (not shown) was nearly superimposable. Therefore, toxic peak plasma levels of side-chain metabolites need not be expected even with short-term infusions, and differences in toxicity and efficacy cannot be explained by an influence of the application time on the metabolic profile.

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A Case of Radiation Myelopathy After 2 × 8.5 Gy For Inoperable Non-small Cell Lung Cancer

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A 56-year old male patient presented in August 1992 with haemoptysis, fever, modest effort dyspnoea and no weight loss. A chest computer tomography (CT) scan showed a mass at the right hilum obstructing the main bronchus and extending to the carina, and a few nodules within the right upper lobe. Bronchoscopy confirmed these findings, and showed a large cell anaplastic carcinoma obstructing the termination of the right main bronchus. On physical examination, he was a robust man for his years, with a blood pressure of 130/75. Blood tests were normal. Bone and CT scan of the brain and abdomen showed no evidence of metastatic disease.

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The patient was treated exclusively with radiotherapy (RT) using an 8 MeV linear accelerator, in the supine position, with AP/PA fields 14.5 × 10 cm^2. A 6 × 3 cm^2 lead triangular shielding was also included supralaterally. The spinal cord was not shielded.

Two fractions of 8.5 Gy (midplane dose (MPD) without lung correction) were given 1 week apart. A radiological partial response of the tumour was observed, and substantial palliation in the patient's symptoms was achieved. The patient remained well until 10 months after radiotherapy when he developed a severe, progressive weakness in the legs and neurological examination revealed a complete Brown–Sequard syndrome at the fifth thoracic level. No sphincter function impairment was noticed. MRI scan showed a heightening of signal in the T2 sequence from T4 to T7, a finding consistent with myelitis (Figure 1).

There was no evidence of spinal cord compression. Bone and brain CT scans were normal. Simultaneously, he developed a tonsillar metastasis which was successfully treated by radical RT. On the last follow-up (November 1994), the patient was completely free of symptoms from both the lung and the tonsil. Both tumours were locally controlled and his neurological status remained stable.

The 2 × 8.5 Gy-1 week apart-scheme has been employed in two randomised studies by the Medical Research Council in the U.K. which compared different palliative schemes for inoperable non-small cell lung cancer (NSCLC). In the first study of 374 patients, one case of radiation myelopathy was suspected (no histological evidence of irradiation damage) [1] while in the second, one case with histologically confirmed radiation myelopathy out of 108 patients was reported [2]. The time for clinical expression of the spinal cord injury was 8 and 17 months, respectively.

In a large retrospective study, Marcus and Million [3] have reported the following rates of radiation myelopathy at each dose level: 0/124 at 30–40 Gy, 0/442 at 40–45 Gy, 2/471 at 45–50 Gy and 0/75 at ≥ 50 Gy. McCunniff and Liang [4] also reported one case of radiation myelopathy among 53 patients who received more than 56 Gy to the cervical spinal cord who were followed-up for more than 2 years. Although cases of radiation myelopathy have been reported with doses below 45 Gy, together with a few cases below 40 Gy, it is possible that all of these may be a result of a dosimetric or other technical error or differences in the RBE (relative biologic efficiency) of orthovoltage beams [3].

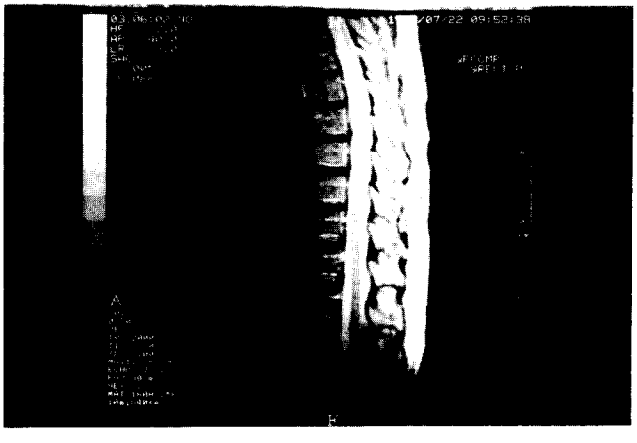

Figure 1. Patient's MRI scan showing a heightening of signal in the T2 sequence.