and acyclovir was administered intravenously (8 mg/kg 3 times daily). Two days after admission, she was oliguric and comatose. She was placed on mechanical ventilation. Creatinemia was 409 μmol/l. Brain TDM and CSF were normal. Plasma acyclovir level measured 12 h after the last administration was 43 μmol/l. After correction of renal impairment with rehydration and furosemide, consciousness returned to normal and the patient was extubated 3 days after admission to the ICU. Plasma acyclovir was then 0.2 μmol/l and creatinemia was 107 μmol/l.

Severe complications of acyclovir affect mainly the brain and the kidney [1]. They are more likely to occur in patients with renal insufficiency [2], acyclovir being eliminated by the kidneys. Nevertheless, overdosing may also occur in patients with only mild renal failure. Neurotoxicity has previously been described even after oral administration [3]. However, deep coma has exceptionally been reported. Plasma acyclovir measurements suggest an overdose and a concentration-adverse effect relationship [4] because the most marked renal abnormalities and abnormalities of consciousness were noticed when the acyclovir level was about 25-fold the upper normal limit for a residual concentration. On the other hand, the return to a therapeutic plasma level coincided with clinical improvement. In this setting, hemodialysis is efficient because it may remove 60% of the body burden of acyclovir [5]. Physicians must avoid these complications of acyclovir by adapting the regimen to renal function and monitoring plasma levels.

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Survival after massive "ecstasy" (MDMA) ingestion

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Sir: The sharp increase in consumption of "ecstasy" (in most cases 3,4-methylenedioxymethamphetamine, MDMA), especially among teenagers and young adults at dance parties or "raves" and "love parades" in and outside Europe, has also increased the number of life-threatening poisonings [1, 2]. Properly, in the last few years special attention has been paid to a number of reported cases of fatal hyperthermic reaction, multiple organ failure MOF and death following ingestion of "ecstasy" due to low amounts of the drug or where low plasma levels were found.

It is well established in the literature that the hyperthermic reaction following ingestion of "ecstasy" apparently is of an idiosyncratic nature [3]. Individual susceptibility may be related to some metabolic predisposition in conjunction with the circumstances in which the drug is used ("raves" – overheating, excessive water loss and lack of compensatory water intake). Published MDMA plasma/serum concentrations in most cases of near fatal or fatal outcome have ranged between 0.11 and 2.1 mg/l [4, 5]. In contrast, no case of poisoning from MDMA with only minimal signs of toxicity but very high serum levels has been reported.

About 12 h after ingestion of a maximum of 40 tablets of "ecstasy" a 19-year-old man (weight 75 kg) was found at home with confusion and central depression and was admitted to an intensive care unit. On admission, he was somnolent, but arousable and cooperative. Blood pressure was 120/75 mmHg. An electrocardiogram showed mild sinus tachycardia (heart rate 95/min). Respiratory rate was 14 breaths/min., body temperature 37 °C. The patient showed normal reflex status, mydriasis and complete retrograde amnesia for 24 h. Common laboratory parameters, especially electrolytes, blood glucose, creatinine, blood cells and parameters of coagulation were within normal ranges. Creatine kinase (CK 366 IU/l) and myoglobin (M) 203 mg/l) were about twice the normal values. In serum, 1.3 g/l ethanol was found.

The results of qualitative and quantitative toxicological analysis using high performance liquid chromatography and gas chromatography-mass spectrometry confirmed the suspected diagnosis. In the first serum sample (Table 1), obtained about 13 h after ingestion, 4.3 mg/l MDMA and, as a metabolite, 0.23 mg/l MDA were found. No other drugs were detected. Initially, after admission, the patient was given 70 g activated charcoal and 0.5 g natrium sulfuricum; 20 mg furosemide was injected intravenously and infusion therapy was started with 1000 ml of Ringer's solution and a 500-ml solution of glucose 6%, each over a period of 2 h and repeated. At control 12 h after admission, CK and M were 462 IU/l and 102 mg/l, respectively. His clinical status improved continuously and he left the hospital against medical advice after 24 h, still with a serum concentration of 0.75 mg/l MDMA!

Reliable diagnosis of "ecstasy" (MDMA) poisoning is made from the case history, clinical situation and qualitative toxicological screening. Quantitative toxi-

Table 1 Concentrations of MDMA in serum and urine (present case)

Time after ingestion (h)[a]	MDMA (serum) mg/l	MDMA (urine) mg/l
13	4.3	630
24	1.4	180
30	0.75	105

[a] approximated time

cological analysis is not considered routinely but is sometimes performed after ingestion of high doses, if severe clinical toxicity is expected or when other drugs need to be excluded. Nevertheless, quantitative toxicological analysis in the individual case is of rather small clinical benefit because there appears to be no sure correlation between acute clinical toxicity and drug level, but there are no data from systematic studies.

Although in the present case severe toxic symptoms in the early phase of poisoning cannot be ruled out definitely, at the time of admission the patient showed only mild symptoms though his MDMA serum level was 4.3 mg/l, which indeed is rarely reported in the literature [1], and confirmed the foreign anamnestic data of ingested amount of tablets. Even if one considers a mitigating central nervous system-effect of ethanol in the present case, which cannot be substantiated from published data, the fact of a serum concentration of 4.3 mg/l without evident clinical symptoms seems to be uncommon. The case reported here shows that clinical toxicity following "ecstasy" overdoses varies considerably among cases and that even extremely high MDMA serum concentrations do not necessarily indicate severe life-threatening poisoning such as hyperthermic reaction and other complications. This case further supports the idea that severe reactions are idiosyncratic and multifactorial and that drug levels have no clinical use except to confirm which agent is responsible.

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Neuromuscular disorders acquired in the ICU

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Sir: De Jonghe et al. are to be complimented for their excellent systematic review on the ICU-acquired neuromuscular disorders (NMD) [1]. However, the exclusion of studies dealing with patients with central nervous system (CNS) diseases may have introduced some biases into their conclusions.

Exclusion was due to the difficulty or impossibility of properly assessing weakness in patients with CNS diseases. However, motor performances can be objectively evaluated, and careful neurologic examination in concert with other investigations may differentiate a deterioration of motor performance due to worsening CNS disease from that caused by ICU-acquired NMD [2]. In our study, all patients who had such an examination were then confirmed to have ICU-acquired NMD [2].

The authors state that the importance of peripheral neurologic abnormalities in comatose patients is unclear. We think that the importance of this is clear when avoiding "unnecessary investigations and unreasonably pessimistic prognosis" is at stake [2]. In our series, physicians predicted that all 24 patients would die "simply" because they attributed the deterioration of motor responses to CNS disease rather than to NMD. In fact, 7 survived, 6 of whom recovered with only minor residual disability. This is particularly important when considering that septic encephalopathy and coma are frequent in the general population of critically ill patients developing NMD [3], a finding that De Jonghe et al. acknowledge.

In the eight studies analyzed, evaluation of the neuromuscular transmission was available in only one study and electromyography (EMG) and muscle biopsy were never performed systematically in the same study. As the authors recognize, this imposes limitations on the interpretation of the results. In fact, not only the neuromuscular blocking agents, but also aminoglycosides, streptomycin, quinidine, verapamil, lidocaine, and several other drugs commonly used in the ICU do interfere with neuromuscular transmission [4]. Furthermore, biopsies or direct muscle stimulation [5] are necessary to diagnose myopathy. Patients in our series all had EMG and neuromuscular transmission studied, and then both muscle and nerve biopsy. The combined interpretation of clinical, electrophysiological, and histologic findings led us to discover that patients had a critical illness myopathy, and that sepsis, not drugs, played a key role [2]. Therefore, the fact that sepsis causes a primary myopathy is no longer a supposition, as De Jonghe et al. suggest.

We fully agree with the author that there is a compelling need for large prospective multicenter studies to define the natural history of ICU-acquired NMD. With the acronym (an acrostic in Italian) of CRIMYNE (critical illness myopathy and neuropathy), such a study is underway in Italy under the aegis of the University of Brescia, the Istituto Mario Negri, and the GiViTI (Gruppo Italiano per la Valutazione degli interventi in Terapia Intensiva). Results should be available in 2001.

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