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5/04

FROM: Steven A. Seifert, MD, Medical Director
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RE: Toxicology Update

The Emergency Department is often the front line in dealing with significant toxic exposures. Here's an update.

1) There's now an **FDA-approved IV form of N-acetylcysteine (NAC), Acetadote®**. It should be available shortly. We still recommend that NAC be given orally as a first line therapy, unless there are contraindications to oral medications, or there is a specific indication for IV NAC. The FDA-recommended protocol is based on the European literature, which is different from the protocol we had been using. The new protocol is for a 20-hour continuous infusion, at varying rates, following a loading dose. We have changed our protocol to follow the FDA's recommendations, for the most part. Where we differ is in our recommendation to continue the infusion for longer than 20 hours in patients who receive their loading dose greater than 8 hours post-overdose. We feel that these patients are at greater risk of hepatotoxicity, that this will not be apparent until 30 to 36 hours, and that there is demonstrated survival benefit of NAC in late presenters with severe toxicity. Thus our recommendation is that IV NAC be continued until the transaminases are negative at 36 hours, in late presenters. If your formulary does not stock the new antidote, we feel it is still acceptable to use the oral form intravenously, according to our protocol, but that there may be additional medico-legal considerations that could come into play should adverse reactions occur. Call us if you would like to be faxed our IV NAC protocol.

2) There is now an **IM form of olanzapine (Zyprexa®)**. Olanzapine is an atypical antipsychotic that is less sedating than haloperidol, droperidol, and possibly ziprazodone (Geodon®). IM Olanzapine is the only such agent that does not prolong the QTc, and thus can more safely be used in the unknown, combative ED patient prior to obtaining an ECG. We still recommend the fewest additional medications in managing acute behavioral problems that may have a toxic-metabolic component. Benzodiazepines would be our first choice for behavioral control. But in the patient who fails to respond to reasonable doses of a benzodiazepine, we recommend IM olanzapine as the next agent. The usual dose is 10 mg IM (2.5 to 5 mg in elderly or debilitated patients). Second and third doses may be given at 2 and 6 hours if needed. Anticipated adverse effects include orthostatic hypotension (0.6%) and bradycardia (0.3%). A 12-lead ECG as soon as possible in these patients is still a good idea, as many will have prolonged QTc's as a result of medications, electrolyte abnormalities (K^+ , Ca^{++} , Mg^{++}), or congenitally, and other ECG effects may also be seen as a result of occult overdoses.