CASE REPORT

The patient was a 2.2 kg, 30-day-old male with a partial airway obstruction secondary to cystic hygromata enlarging in the floor of the mouth and subcutaneously throughout the anterior neck. He was brought to the operating room for emergency resection of these rapidly enlarging masses. After he was given atropine sulphate 0.1 mg, anaesthesia was induced with halothane and then maintained with 50% nitrous oxide in oxygen by controlled ventilation facilitated by tubocurarine 1.7 mg. After 5 hours of surgery the curare was reversed with neostigmine 0.25 mg mixed with atropine sulphate 0.1 mg, and the nitrous oxide was discontinued. The only other medications that the patient had received that day were ampicillin 100 mg and dexamethasone 1 mg. The child was returned to the recovery room with a nasal endotracheal tube in place.

Upon arrival in the recovery room, the patient's respiration was spontaneous and regular. He had a normal sinus arrhythmia with a rate of 140/min, and his rectal temperature was 36.1°C. He was lethargic but initially responsive to simple stimuli with eye opening and sucking. He developed some intermittent shaking movements which increased in duration and frequency over the first 2-3 postoperative hours to a severe opisthotonic-type seizure activity. By 3½ hours he was in a state of near status-opisthotonos. During this time his temperature had increased to 37.1°C. His pulse had slowed from 140 to 120 beats/min, and his breathing had become irregular with periods of apnoea lasting up to 15 sec in duration. His pupils, noted to be widely dilated for 2 more days; otherwise the remainder of his heart rate was 140 beats/min and regular. Physostigmine 0.035 mg was then given. The seizures stopped and the child began to waken. However, he also developed wheezing breath sounds, hypersalivation, marked hyperperristalsis, and his heart rate slowed to less than 100 beats/min. It was felt that these symptoms were the result of peripheral cholinergic (muscarinic) overstimulation secondary to the physostigmine. Glycopyrrolate 0.02 mg, an anticholinergic which does not readily penetrate the blood brain barrier, was given i.v. to block the peripheral effects of the physostigmine. Within 3 min the wheezing had stopped; the child's mouth was dry again; his abdomen was calm; and the heart rate was 140 beats/min and regular. Physostigmine 0.07 was then given. Within 2 min the child was alert, crying, sucking, and looking about. The pupils remained dilated for 2 more days; otherwise the remainder of his stay in hospital was unremarkable.

DISCUSSION

Atropine toxicity has been known since the Middle Ages, when it was used to produce obscure and often prolonged poisoning (Innes and Nickerson, 1970). Its manifestations range from lethargy, drowsiness, and possible hyperthermia to delirium, hallucinations, coma, convulsions, and death (Ritte, 1926; Heath, 1950; Morton, 1939; Hoefnagel, 1961; Forrer and Miller, 1958; Alexander, Morris and Eslick, 1946). Death in children from atropine poisoning has been reported with doses as small as 0.05 mg/kg (Ritte, 1926) and 0.2 mg/kg (Morton, 1939; Hoefnagel, 1961). There are reports of coma and convulsions in children with doses in the region of 0.5 mg/kg (Hoefnagel, 1961; Morton, 1939).

The patient in this case report received a combined pre- and postoperative dose of just less than 0.1 mg/kg; yet psychiatrists in the past have used atropine for coma therapy in adults in doses ranging
from 0.5 to 3.0 mg/kg (Forrer and Miller, 1958). Recovery has been noted in one adult after the ingestion of 1 g of atropine (Alexander, Morris and Eslick, 1946).

The belladonna alkaloids, atropine, hyoscine and homatropine, which are associated with the central anticholinergic syndromes, all possess a tertiary-amine, non-ionized molecule which allows easy passage across the blood brain barrier. The short-acting anti-cholinesterase physostigmine is a tertiary-amine also and readily passes the blood brain barrier. On the other hand, neostigmine, pyridostigmine and edrophonium chloride are ionized quaternary-ammonium compounds and do not readily cross the blood brain barrier. Therefore, while the tertiary-amine anticholinergic, atropine, will have mutual peripheral muscarinic antagonism with neostigmine, its central anticholinergic activity can only be antagonized by an anticholinesterase, such as physostigmine, which has similar passage of the blood brain barrier.

The synthetic anticholinergic, glycopyrrolate, which is an ionized quaternary-ammonium compound does not cross the blood brain barrier. It is for this reason that, when the child developed symp-

toms of peripheral cholinergic overdose after the second dose of physostigmine, glycopyrrolate was used. It reversed the muscarinic effects of the cholinergic drug overdose but did not contribute to any further central anticholinergic depression.

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REFERENCES