Anesthesiology
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In Reply:—Wingard brings up the possibility that our patient might have manifested central and peripheral effects caused by ranitidine and glycopyrrolate, respectively. However, as stated in the review he quotes of cimetidine, central nervous system (CNS) symptoms are more frequent in the extremes of age, with high doses, and in patients with either or both renal or liver disease where an increased cerebrospinal fluid/plasma cimetidine ratio has been found.[1] Indeed, both patients in the case report[2] he cited appear to fit these criteria: they were taking 300 mg cimetidine intravenously every 6 h (one for 3 days, and the other for "several doses"), and one (age 58 yr) had congestive heart failure, hepatomegaly, and prerenal azotemia, while the other (age 60 yr) had heart failure, bacterial endocarditis, and renal insufficiency. Our patient was 22 yr old and perfectly healthy, and received a single, properly administered intramuscular dose of ranitidine. Ranitidine, in contrast to cimetidine, is minimally distributed in the CNS, has different brain receptor binding characteristics, and does not appear to have the same severe degree of CNS side effects.[3]

The change in cardiovascular parameters secondary to glycopyrrolate in the cited study by Skues *et al.*[4] are in no manner comparable to what we observed in our patient. In their patients, systolic and diastolic blood pressures each increased by about 5 mmHg, and heart rate accelerated by about 15 beats per min. Both systolic and diastolic pressures were trending downward within 5 min after administration. The peak changes in our patient were a systolic pressure increase of 65 mmHg, a diastolic pressure increase of 46 mmHg, and an increase in heart rate of 64 beats per min. These changes were unrelenting until physostigmine administration.

Thus, the drug (ranitidine *versus* cimetidine), the extent of central nervous system response, the baseline physiologic state, and the cardiovascular manifestations of our patient do not seem to be comparable to those in the articles Wingard cites. Although the possibility of drug interaction remains, we suggest that the finding of Proakis and Harris[5] that glycopyrrolate's penetration across the blood–brain barrier is poor, but not absent, should well be heeded.

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Applications of Molecular Genetics to Anesthesiology

To the Editor:—The editorial by Levitt *et al.*[1] praises the talents of geneticists, molecular biologists, biochemists, and anesthesiologists as they are being applied to unraveling the mysteries of malignant hyperthermia. I should like to offer my own homage to that effort and commend the work of MacKenzie *et al.*[2] in attempting to reconcile the caffeine–halothane muscle contracture test with the proposed molecular genetic abnormality of malignant hyperthermia.

The practical applications of molecular genetics have been clearly established in the specialty of anesthesiology in recent years.[3] Regrettably, none of this seminal work has appeared in the anesthesia literature. Human serum cholinesterase (butyrylcholinesterase) has recently been sequenced and cloned by Lockridge *et al.*[4] McTiernan *et al.*[5] determined that cholinesterase isolated from fetal brain is identical in its amino acid sequence as serum cholinesterase. McGuire *et al.*[6] identified the structural mutation responsible for the dibucaine-resistant (atypical) variant form of human serum cholinesterase. Identification of a frameshift mutation responsible for the silent phenotype of human serum cholinesterase was reported by Nogueira *et al.*[7]

Application of DNA structural analysis methodology allows for the precise characterization of the numerous (at last count, 13) serum cholinesterase variants, many of which would be extremely difficult or impossible to differentiate using the traditional chemical inhibitory techniques.*

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