Neuromuscular Effects of Beta-adrenergic Blockers and Their Interaction with Skeletal Muscle Relaxants

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Intra-arterial pronethalol and propranolol produced a short-lasting neuromuscular blockade in the soleus nerve-muscle preparation of the cat. Intravenous pronethalol and propranolol prevented repetitive potentials of the soleus nerve as well as twitch potentiation and fasciculations of the soleus muscle induced by intravenous succinylcholine, but potentiated neuromuscular blockade. MJ 1999 did not protect fully against succinylcholine stimulation. Curare, 200-350 µg/kg, intravenously produced partial-to-complete neuromuscular blockade which was potentiated by intravenous pronethalol or propranolol. No significant potentiation was induced with corresponding doses of MJ 1999. We conclude that the neuromuscular effects of beta-adrenergic blockers are independent of their interaction with catecholamines. The prevention of succinylcholine-induced potentials is ascribed to a presynaptic effect of beta blockers which depends on the "local anesthetic" activity of the drugs.

**Beta-adrenergic blocking agents** have proved effective against a variety of experimentally-induced cardiac arrhythmias. Early studies 1-4 have demonstrated that these drugs have a twofold action; in small doses, they counteract arrhythmias induced by sympathomimetic amines, whereas in larger doses, arrhythmias induced by digitalis glycosides are antagonized. The former effect has been related to blockade of the beta-adrenergic receptors, whereas the latter has been linked to an unspecified "quinidine-like" or "local anesthetic-like" effect on the heart.

Because larger doses of sympathetic beta-blocking agents also affect other excitable tis-

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the interaction of these agents with the skeletal neuromuscular blockers, succinylcholine and curare.

Methods

The experiments were performed in cats anesthetized with 80 mg./kg. chloralose, intravenously. The methods employed are illustrated in figure 1. Basically, they included recording of the soleus muscle twitch tension and soleus nerve action potentials. The former is a fundamental pharmacologic technique for the study of neuromuscular transmission; the latter method, developed by Riker et al.16 and Standaert 17 permits assessment of function of the nerve terminal. When a nerve is stimulated either electrically or by drugs, an action potential is propagated throughout the axon—orthodromically as well as antidromically—and can be recorded at any point on the axon. The experiment is performed most conveniently on a ventral spinal nerve root.

The popliteal fossa was dissected to expose the soleus muscle, with its nerve and blood supply. The isometric contraction of the soleus muscle in response to supramaximal shocks applied to the sciatic nerve (2.5 sec. interval, 0.5 msec. duration) was recorded on a Texas oscillograph. In selected experiments, a lumbar laminectomy was performed to expose the L7 ventral root, the origin of the soleus nerve. The root was detached from the spinal cord and subdivided until a filament containing a single active axon was located. This was placed on a bipolar recording electrode. Nerve potentials from the single axon were displayed on a Tektronix oscilloscope and photographed. The popliteal fossa and lumbar region, held open by sutured retention cords, were filled with paraffin oil equilibrated with 95 per cent O2-5 per cent CO2. Temperature was maintained at 37° C. with a regulated heat lamp. A tracheotomy was performed. When necessary, ventilation was assisted with a Harvard pump respirator. Arterial blood pressure and pulse in the carotid artery were recorded via an indwelling catheter and a Statham pressure transducer connected to the Texas oscillograph.

Drugs: Pronethalol, propranolol, MJ 1999, succinylcholine and d-tubocurarine were dissolved in saline solution and the concentrations adjusted so that the dose per kilogram was 0.1 ml. intra-arterially or 1 ml. intravenously. In five experiments, increasing doses of a given beta blocker were injected into the popliteal artery at 30-minute intervals and a dose-response relationship of the soleus muscle twitch tension depression was determined. In all other cases, drugs were injected into the external jugular vein. In 20 experiments, the beta blockers were administered between two doses of succinylcholine; in 15, they were given during the recovery phase of a curare-induced paralysis. The degree of sympathetic beta blockade was tested with 0.5 μg/kg. isoproterenol administered intravenously.

Results

CLOSE INTRA-ARTERIAL INJECTION OF
BETA BLOCKERS

Increasing doses of pronethalol and propanolol induced brief depression of the indirectly-stimulated twitch; pronethalol 5.5 mg./kg. and propranolol 4.7 mg/kg. effected a 50 per cent block (ED50). The difference between these doses was not significant (P > 0.2). Following a one-to-three minute partial paralysis, the muscle regained its initial tension. On three occasions, however, a twitch potentiation lasting from five to 16 minutes developed following recovery from
neuromuscular blockade induced by propranolol. In these instances, twitch potentiation was unaccompanied by repetitive potentials in the motor nerve terminals, such as those which occurred following twitch potentiation resulting from succinylcholine administration (see below). In contra-distinction to pronethalol and propranolol, corresponding doses of MJ 1999 did not affect twitch tension of the soleus muscle. The intra-arterial injection of beta blockers caused a fall in systolic blood pressure (10–30 mm. Hg), and/or a slight decrease in heart rate (10–30 beats per minute).

**Intravenous Administration of Beta Blockers**

The intravenous administration of as much as 20 mg./kg. pronethalol or propranolol or 40 mg./kg. MJ 1999 was not followed by decrease in the soleus muscle twitch tension (figs. 2 and 3). All drugs, however, antagonized the positive chronotropic effect of isoproterenol on the heart (table 1). In equal mg. per kg. doses, MJ 1999 was roughly two times and propranolol ten times more potent as chronotropic beta blocking agents than pronethalol. The largest doses of the three drugs resulted in moderate arterial hypotension.

**Intravenous Administration of Succinylcholine and Beta Blockers**

Intravenous succinylcholine (10–50 μg./kg.) produced widespread muscle fasciculations, potentiation of the soleus muscle twitch tension and repetitive action potentials recorded from the L7 ventral root filament (fig. 4). These excitatory effects lasted 20 to 60 seconds. Larger doses of succinylcholine caused similar initial effects, and in addition, precipitated 30–100 per cent neuromuscular blockade that appeared within 30 seconds and persisted for as long as five minutes. All neuromuscular effects of succinylcholine were fairly consistent for the same animal when the injections were done at 20- to 30-minute intervals.

Intravenous pronethalol, 2.5 to 10 mg./kg., prior to administration of succinylcholine prevented repetitive firing of the soleus nerve, as well as fasciculations and twitch potentiation of the soleus muscle. The magnitude and duration of neuromuscular blockade induced by succinylcholine, however, was increased 20–40 per cent. When partial neuromuscular blockade was induced by succinylcholine, a fall in systolic blood pressure (10–30 mm. Hg) and/or a slight decrease in heart rate (10–30 beats per minute) was observed. Isoproterenol, 0.5 mg./kg., injected at arrow, had no effect on the systolic blood pressure in these experiments. When the dose was increased to 1.0 mg./kg., a fall in systolic blood pressure (10–30 mm. Hg) and/or a slight decrease in heart rate (10–30 beats per minute) occurred. Isoproterenol, 0.5 mg./kg., injected at arrow, had no effect on the systolic blood pressure in these experiments. When the dose was increased to 1.0 mg./kg., a fall in systolic blood pressure (10–30 mm. Hg) and/or a slight decrease in heart rate (10–30 beats per minute) occurred. Isoproterenol, 0.5 mg./kg., injected at arrow, had no effect on the systolic blood pressure in these experiments. When the dose was increased to 1.0 mg./kg., a fall in systolic blood pressure (10–30 mm. Hg) and/or a slight decrease in heart rate (10–30 beats per minute) occurred.
### Table 1. Neuromuscular and Systemic Effects of Pronethalol, Propranolol and MJ 1999*

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Pronethalol</th>
<th>Propranolol</th>
<th>MJ 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression of indirectly</td>
<td>Minimal effective dose</td>
<td>None up to</td>
<td>None up to</td>
<td>None up to</td>
</tr>
<tr>
<td>elicited twitch</td>
<td>20 mg./kg.</td>
<td>20 mg./kg.</td>
<td>20 mg./kg.</td>
<td>40 mg./kg.</td>
</tr>
<tr>
<td>50 per cent block (E D 50)</td>
<td>5.5 mg./kg.</td>
<td>(6)</td>
<td>(8)</td>
<td>(6)</td>
</tr>
<tr>
<td>Potentiation of curare</td>
<td>minimal effective dose</td>
<td>2.5 mg./kg.</td>
<td>2.5 mg./kg.</td>
<td>40 mg./kg.</td>
</tr>
<tr>
<td>paralysis</td>
<td></td>
<td>(4)</td>
<td>(4)</td>
<td>(7)</td>
</tr>
<tr>
<td>Antagonism of succinylcholine</td>
<td>Minimal effective dose</td>
<td>2.5 mg./kg.</td>
<td>2.0 mg./kg.</td>
<td>30 mg./kg.</td>
</tr>
<tr>
<td>stimulation</td>
<td></td>
<td>(6)</td>
<td>(8)</td>
<td>(6)</td>
</tr>
<tr>
<td>Antagonism of isoproterenol</td>
<td>75 per cent block (E D 75)</td>
<td>3.1 mg./kg.</td>
<td>0.3 mg./kg.</td>
<td>1.5 mg./kg.</td>
</tr>
<tr>
<td>tetanyardia</td>
<td></td>
<td>(11)</td>
<td>(14)</td>
<td>(11)</td>
</tr>
<tr>
<td>Potentiation of curare/</td>
<td>Dose ratio</td>
<td>0.8:1</td>
<td>8.3:1</td>
<td>26.6:1</td>
</tr>
<tr>
<td>antagonism of isoproterenol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Figures in parenthesis = number of experiments done.
† Intravenous administration; in all other instances, drugs were injected intravenously.

Muscular block was achieved with succinylcholine, intravenous pronethalol or propranolol caused further reduction of twitch height. The more intense the blockade, the smaller was the dose of pronethalol or propranolol required to affect neuromuscular transmission (fig. 5). In doses as large as 30 mg./kg. MJ 1999 did not have the modifying effects of the other beta blockers. Slight prolongation of the neuromuscular blockade and partial prevention of the stimulatory effects of succinylcholine were observed with doses of 30-40 mg./kg.

**Intravenous Administration of Curare and Beta Blockers**

Intravenous administration of 200-350 µg./kg. curare resulted in 40 to 100 per cent neuromuscular blockade, which was not preceded by stimulation. Recovery to control twitch occurred within 15 minutes. In contrast to succinylcholine, successive doses of curare had a marked cumulative effect. For this reason, beta blockers were tested only during the recovery period of curare-induced paralysis. Thus, intravenous pronethalol and propranolol increased the magnitude and duration of curare block in a dose-related fashion (fig. 6). Minimal effective doses of pronethalol or propranolol were 2.5 mg./kg. The effect of either drug in 5 mg./kg. doses was roughly equivalent to the effect of 50 µg./kg. curare. Tested in the same fashion, MJ 1999 had only a slight neuromuscular depressant effect at the 40 mg./kg. dose level.

**Discussion**

The present experiments have demonstrated that intravenous pronethalol, propranolol and MJ 1999 antagonize isoproterenol and differentially modify the neuromuscular effects of succinylcholine and curare. The same dose of pronethalol effectively produced both beta-adrenergic and neuromuscular blockade. On the other hand, neuromuscular blocking doses of propranolol and MJ 1999 were 8 and 25 times greater, respectively, than the beta blocking doses. The durations of action of beta blockade and neuromuscular depression also were independent: neuromuscular blockade persisted for a few minutes, whereas antagonism of isoproterenol continued for several hours. Thus, from both the dose-response and the time-action curves, it appears that myocardial effects of beta-adrenergic drugs are unrelated to their interaction with catecholamines. This conclusion was not unexpected.
not be held primarily responsible for the present results. Intra-arterial pronethalol and propranolol depressed neuromuscular transmission while reducing the arterial blood pressure only slightly. MJ 1999 had a minimal neuromuscular effect despite producing arterial hypotension.

INTERACTION ON PLASMA PROTEINS AND PLASMA CHOLINESTERASE

Approximately 70 per cent of d-tubocurarine present in the blood stream is bound loosely to protein, presumably to plasma albumins. The remaining 30 per cent circulates in free plasma water. Since the unbound drug is in equilibrium with muscle relaxant at the neuromuscular junction, the unbound fraction represents the pharmacologically-active drug. A variety of agents used during surgery and anesthesia, including local anesthetics, can displace muscle relaxants from plasma proteins, thus increasing their concentration at the myoneural junction. Whether beta blockers are capable of displacing curare from plasma proteins remains to be determined. The alternative possibility for drug potentiation applies to succinylcholine only. Since succinylcholine is metabolized by plasma cholinesterase, it is possible that beta blockers prolong succinylcholine paralysis by enzymatic inhibition, but this is unlikely. In other experiments, we did not find significant reduction of the splitting activity of plasma cholinesterase incubated with $10^{-5}$ to $10^{-4}$ concentrations of pronethalol, propranolol or MJ 1999. It should be noted that these in vivo concentrations of beta blockers are somewhat higher than those expected in vivo following the injection of experimental doses.

INTERACTION AT THE NEUROMUSCULAR JUNCTION

Drugs can interfere with neuromuscular transmission by affecting presynaptic and/or postsynaptic structures. For example, it is agreed generally that the hemicholiniums act on nerve terminals, that neuromuscular blockers act on postsynaptic membranes, and that magnesium affects both. Within the past few years, however, it has been shown that several effects of skeletal muscle relaxants
may be induced by drug action at presynaptic sites. An example of such presynaptic effects is the appearance of repetitive potentials immediately following the injection of succinylcholine. The neural origin of these potentials is supported mainly by two observations: they always precede corresponding potentials in the muscle, and they have a completely independent dose-relation and time course in relation to other effects of succinylcholine (for instance, to neuromuscular blockade). Recognition of this stimulatory action on the nerve terminal is important since it explains the muscle fasciculations and twitch potentiation induced by administration of succinylcholine. The arrival of succinylcholine at individual motor units is not uniform because of delay in transportation of the drug by the bloodstream. The uncoordinated stimulation of motor nerve endings causes individual muscle fibers to contract asynchronously; thus, muscle fasciculations occur. On the other hand, repetitive potentials in the nerve change the single electrical stimulus into a brief tetanus, prolonging the active state of the muscle, and thus, producing the twitch potentiation. The demonstration of a presynaptic origin of stimulatory effects of succinylcholine has another important implication. Since repetitive potentials are neural events and beta blockers depress them without depressing the transmission of single twitches, beta blockers must act by selective depression of the motor nerve terminal.

Results of the present experiment have demonstrated that neuromuscular effects of beta blockers do not depend on interaction with catecholamines; instead, they seem to depend on the nonspecific or “local anesthetic” effect of these drugs. There is evidence to support this assumption. In general, the neuromuscular effects of beta blockers strikingly resemble those of local anesthetic compounds, in that both groups can produce neuromuscular block-

Fig. 5. Effect of intravenous propranolol on neuromuscular paralysis by succinylcholine. A. Intravenous injection 100 μg/kg. succinylcholine produced partial neuromuscular blockade preceded by twitch potentiation. B. 30 minutes later, 5 mg/kg. intravenous propranolol injected before the administration of 100 mg/kg. succinylcholine. More prolonged, longer-lasting neuromuscular blockade not preceded by potentiation resulted. C. Thirty minutes after B, a third dose, 100 mg/kg. succinylcholine, produced twitch potentiation and neuromuscular blockade. D. Intravenous propranolol, 1 mg/kg. injected during the recovery phase from succinylcholine-induced paralysis, did not curtail muscle power appreciably. E. Intravenous propranolol, 1 mg/kg. injected during an earlier phase of recovery from succinylcholine-induced paralysis, produced 100 per cent neuromuscular blockade.
ade; they present the initiation of repetitive potentials, twitch potentiation and muscle fasciculations induced by succinylcholine, and they prolong muscle paralysis induced by skeletal neuromuscular blockers.24, 25, 26 More specifically, pronethalol and propranolol are also local anesthetics with potencies approximating that of lidocaine.5, 7 Therefore, the observation that pronethalol and propranolol are equally potent myoneural depressants is in accord with what is known about the local anesthetic potency of these drugs. Furthermore, MJ 1999, a weak myoneural depressant is almost devoid of any local anesthetic effect.14, 15 The striking similarity between the effects of beta blockers and local anesthetics on the motor nerve terminal is not restricted to this portion of the nervous system. Given intravenously, both groups of drugs can depress spinal reflexes,5, 27 prevent cardiac arrhythmias and vomiting due to digitalis,5, 28 prolong barbiturate anesthesia, and produce generalized convulsions in the experimental animal.1 Thus, the effects at motor nerve terminals are another example of the generalized neural actions of the drugs.

Unlike the suppression of repetitive potentials, which can be pinpointed as a prejunctional effect, the explanation for other neuromuscular effects of beta blockers is rather unsatisfactory. One of the phenomena difficult to explain is the twitch potentiation that occasionally followed administration of propranolol. Because there were no repetitive potentials in the nerve, this can be suspected of being due to a drug effect on the muscle fiber. In this regard, it is pertinent to recall that antiarrhythmic drugs such as quinidine can increase the peak tension of skeletal muscles by slowing the propagation of the action potential along the muscle fiber, that is, by prolonging the duration of the active state. The second debatable subject is the mechanism of neuromuscular blockade. In the two studies previously describing the effect, Turker and Kiran 2 postulated a reduction of transmitter output, whereas Standaert et al.8 envisaged a further depression of nerve terminals as the cause of neuromuscular blockade. Since we have no new evidence to present and our knowledge of neuromuscular depression by beta blockers is incomplete (for instance, the endplate potential has not yet been determined), further discussion of the subject would be noncontributory.

The clinical significance of these results deserves comment. Although species differences preclude authoritative conclusions, we do not believe that small doses of beta blockers will depress the muscle strength of normal individuals or prolong the effect of curare during general anesthesia. Normally the most important and dangerous effects of beta-adrenergic blocking agents occur in relation to the circulation. However, certain patients with muscle dysfunction undergo anesthesia and operation. Some myasthenic patients manifest irregularities of cardiac rhythm 25, 26 which often are treated with local anesthetic injections, quinidine, or procainamide. The administration of antiarrhythmic drugs to these patients occasionally has resulted in aggravation of their weakness.21, 22 For that reason, the injection of drugs such as pronethalol, in which the beta blocking and the "local anesthetic" actions occur within the same dose range, is potentially hazardous. In myasthenic patients the use of drugs exhibiting the widest divergence between the beta-adrenergic and the myoneural depressant doses, such as propranolol or MJ 1999, would appear more desirable. Finally, the prevention of the stimulatory effects of succinylcholine by some beta blockers should be considered. Because pronethalol and propranolol share these properties with local anesthetics, it is possible that beta blockers can also prevent the postoperative muscle pain induced by succinylcholine administration.23 A careful postoperative follow-up of patients who have received beta blockers could provide this information.

Summary

The neuromuscular effects of the beta-adrenergic blocking agents pronethalol, propranolol and MJ 1999 were studied in the soleus nerve-muscle preparation of the cat. The beta blocking effects of these drugs were assessed by the intravenous injection of isoproterenol. Intra-arterial administration of pronethalol and propranolol resulted in a dose-dependent, short-lasting neuromuscular block-
Fig. 6. Effect of intravenous propranolol on curare-induced paralysis. 
A. Intravenous propranolol, 1 mg/kg, had no effect on twitch tension 
of the soleus muscle during recovery from the effect of 200 µg/kg dose of 
curare. B. Intravenous propranolol, 5 mg/kg, potentiated and prolonged 
the neuromuscular depression produced by 250 mg/kg curare.

The ED₅₀ of prOthalol was 5.5 mg/kg and that of propranolol 4.7 mg/kg. 
Corresponding doses of MJ 1999 had no appreciable effect on neuromuscular transmission. 
The intravenous administration of beta blockers was not followed by any reduction of the twitch tension, despite demonstration of long-
lastingly beta-adrenergic receptor blockade.

Succinylcholine, 10–50 µg/kg, intravenously, induced repetitive potentials of the soleus nerve, muscle fasciculations and twitch potentiation. Larger doses caused the same initial stimulatory effects followed by neuromuscular blockade. Administration of pro-
Othalol or propranolol prior to succinylcholine prevented repetitive potentials of the nerve and the fasciculations, as well as twitch potentiation in the muscle, but potentiated the neuromuscular blockade. MJ 1999 did not protect fully against succinylcholine stimulation.

Curare, 200–350 µg/kg, intravenously, produced partial-to-complete neuromuscular blockade which was potentiated by intravenous pro-
Othalol or propranolol. No significant potentiation was induced with corresponding doses of MJ 1999.

On the basis of the dose-effect and the time-action relationship, we conclude that neuromuscular effects of beta blockers are independent of their interaction with catecholamines; rather, neuromuscular effects depend on "local anesthetic" activity of the drugs. For this reason, the use of beta blocking agents with high local anesthetic potency is considered hazardous in patients with neuromuscular dysfunction. The prevention of succinylcholine-induced repetitive potentials, muscle fasciculations and twitch potentiation is ascribed to a presynaptic effect of beta blockers. The site of the other actions is unknown.

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. References

6. Sekiya, A., and Vaughan Williams, E. M.: Central and peripheral actions of prometha- 
7. Tucker, K., and Kiran, B.: Action of prometha- 
lol on neuromuscular activity, Arch. Int. 
8. Standaert, F. G., Levitt, B., and Roberts, J.: 
Antagonism of digitals arrhythmias by pro- 
methanol—a nerval phenomenon? Nature 
210: 742, 1966.
9. Lucchesi, B. R., Whitsett, L. S., and Brown, 
N. L.: Propranolol (Inderal) in experiment- 
tally induced cardiac arrhythmias, Canad. 
effects of propranolol, Amer. J. Cardiol. 18: 
468, 1966.
11. Hewitt, P. B., Lord, P. W., and Thornton, 
H. L.: Propranolol in hypotensive anesthe- 
during controlled hypotension, Brit. J. 
halothane anesthesia, Brit. J. Anaesth. 38: 
516, 1966.
14. Lash, P. M., Toikel, J. H., and Dungan, K. 
W.: Pharmacological and toxicoological prop- 
erties of two new #-adrenergic receptor an- 
tagonists, J. Pharmacol. Exp. Ther. 149: 
15. Somani, P., Fleming, J. G., Chan, K. K., and 
Lum, B. K. E.: Antagonism of epinephrine- 
induced cardiac arrhythmias by 4 (3- 
propylamine-1-hydroxyethyl) methane-sulfon- 
16. Riker, W. F., Jr., Roberts, J., Standaert, F. G., 
and Fujimura, H.: The motor nerve terminal 
as the primary focus for drug induced facilita- 
tion of neuromuscular transmission, J. 
17. Standaert, F. G.: Post-tetanic repetitive activ- 
ity in the cat soleus nerve, J. Gen. Physiol. 
18. Del Santo, G.: Kinetics of distribution of 
radioactive-labelled muscle relaxant. I In- 
vestigations with Cs dimethyl-d-tubocurara- 
19. Usuiaga, J. E., Wilkins, J. A., Morales, R. 
L., and Usuiaga, L. E.: Interaction of 
intravenously-administered procaine, lidoca- 
ine and succinylcholine in unanesthetized 
21. Hofmann, W. M.: The pharmacology of the 
hemicholinium, Ann. N. Y. Acad. Sci. 135: 
276, 1966.
22. Widmer, C.: Magnesium on neuromuscular 
23. Standaert, F. G., and Adams, J. E.: The ac- 
tions of succinylcholine on the mammalian 
motor nerve terminal, J. Pharmacol. Exp. 
24. Usuiaga, J. E., Wilkins, J. A., Wilkins, R. 
L., and Usuiaga, L. E.: Prevention of succi- 
nylcholine fasciculation with local anes- 
thetics, Anesthesiology 26: 3, 1965.
25. Usuiaga, J. E.: Effect of local anesthetics on 
the myoneural junction (correspondence), 
26. Usuiaga, J. E.: Presynaptic effects of local 
anesthetic agents at the myoneural junction, 
27. Petersen, C. G.: Neuropharmacology of pro- 
caine: II. Central nervous actions, Anes- 
28. Usuiaga, J. E., Moya, F., Wilkins, J. A., 
and Usuiaga, L. E.: Efeito da lidocaína, 
prilocaine, difenhidramina e promethanol 
as arritmias digitais e sua relação com o 
bloqueio dos receptores beta-adrenérgicos, 
29. Ask-Upmark, E.: Cardiovascular observations 
in myasthenia gravis and dystrophia myo- 
30. Oserman, K. E.: Myasthenia gravis. New 
— a hazard in myasthenia gravis, Arch. 
32. Weisman, S. J.: Masked myasthenia gravis, 
33. Usuiaga, J. E., Wilkins, J. A., Usuiaga, 
L. E., and Molina, F.: Intravenous lidocaine 
in the prevention of postoperative muscle 
pain caused by succinylcholine administra- 

Erratum

In the article "Metabolism of Drugs Employed in Anesthesia," which ap- 
ppeared in the March–April issue (Anesthesiology 29: 332, 1968), the sen- 
tence "The only important oxybarbiturate not excreted unchanged is barbital" 
(p. 332, right-hand column) should read "The only important oxybarbiturate 
excreted unchanged is barbital."