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Hypermetabolism Precipitated by a Monoamine Oxidase Inhibitor

To the Editor:—It was with great interest that we read the report by Caroff *et al.* describing the biochemical similarities and dissimilarities between patients with malignant hyperthermia susceptibility and neuroleptic malignant syndrome.[1] It was most interesting to note the results of the authors' fluphenazine contracture test as a pharmacological model for inducing muscle contracture *in vitro*. The authors' results, however, suggested that the *in vitro* contracture response to fluphenazine did not correlate with clinical evidence of neuroleptic malignant syndrome or malignant hyperthermia susceptibility.

In an earlier case report, we described a rare case of an overdose to a monoamine oxidase inhibitor (MAO) whereby the patient developed a hypermetabolic state not unlike that found in neuroleptic malignant syndrome or malignant hyperthermia.[2] This patient also recovered after treatment with dantrolene sodium. A muscle biopsy performed at a later date revealed no pathology or abnormal fiber type distribution and a negative response to halothane and caffeine contracture test according to criteria established by Rosenberg and Reed.[3] The muscle, however, did contract when bathed in 10^{-5} molar concentration of another MAO inhibitor, pargyline. It is because of this finding that we are most curious as to whether the authors of this paper might have also tested the muscle specimens from their patients to this class of drug. If not, we feel that further investigation with this class of drug might prove fruitful in determining the mechanism by which these psychotropic drugs produce bizarre hypermetabolic reactions.

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In Reply:—We appreciate the interest of Dr. Feinglass in our article on the relationship between neuroleptic malignant syndrome (NMS) and malignant hyperthermia (MH).[1] In our study, we found that five of seven NMS patients tested positive for MH-susceptibility based on the *in vitro* contracture response of skeletal muscle to halothane. As we indicated, the clinical significance of these findings depends on the specificity of the halothane-contracture test, particularly in patients with prior muscle pathology. We also found that fluphenazine-induced contractures did not correlate with MH or NMS susceptibility, and, therefore, may not be relevant to mechanisms underlying these disorders.

We did not examine muscle effects of other psychotropic drugs, although, as the intriguing report by Dr. Feinglass *et al.*[2] suggests, other drugs are associated with hypermetabolic syndromes which may differ from MH in etiologic mechanisms. These investigators reported the development of hyperthermia (41° C), muscle rigidity, coma, tachycardia, hypoxia, hypercapnia, metabolic acidosis, and rhabdomyolysis in a 33-year-old patient who ingested a toxic dose of phenelzine, a monoamine oxidase inhibitor, in an apparent suicide attempt. These symptoms responded dramatically to intravenous dantrolene sodium (2.5 mg/kg), and the patient recovered. On subsequent *in vitro* testing, a normal contracture response to halothane and caffeine, and normal muscle histology were found, indicating that the patient was not MH-susceptible and that the mechanisms underlying this reaction probably differed from those involved in MH. However, muscle from this patient did contract in response to pargyline (10^{-5} M), another monoamine oxidase inhibitor.

While it is difficult to interpret the response to pargyline in the absence of control data, the therapeutic response to dantrolene underscores the similarities be-

tween the various drug-induced hypermetabolic syndromes.[3] Although these reactions probably have distinct pharmacologic mechanisms, with psychotropic drugs acting primarily on central structures, they appear to culminate in a common dantrolene-responsive disturbance of skeletal muscle contractile and energetic properties, resulting in rigidity and hyperthermia.

We join with Dr. Feinglass in encouraging additional investigations of these drug-induced syndromes. However, we recommend that investigators consider the range of drug effects on central, as well as peripheral, components of the neuromuscular and thermoregulatory systems, and urge that future reports specify details on subjects, procedures, results, and control groups to facilitate comparisons between studies.

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Axillary Block of the Brachial Plexus: "You Can't Get There From Here . . ."

To the Editor:—Selander's editorial, "Axillary Plexus Block: Paresthetic or Perivascular," attempts to answer the question "How should an axillary block be performed?."[1] Selander oversimplifies the issue by claiming the superiority of single-injection techniques over elicited-paresthesia techniques with multiple injections of local anesthetic agent. However, many anesthesiologists utilize multiple injections with the aid of an electrical nerve stimulator, locating specific nerves by eliciting an electrically induced evoked motor response without a sensory paresthesia (motor threshold is lower than sensory). Selander supports his claim with studies by himself[2] and Plevak *et al.*[3] suggesting that the paresthesia technique for axillary block increases the incidence of postanesthetic neuropathy. In fact, there was no statistically significant difference in the incidence of postanesthetic neuropathy with or without paresthesias in either publication. Is the paresthesia technique associated with a higher incidence of postanesthetic neuropathy? Winchell and Wolfe* published prospective data showing only a 0.36% incidence of post-block neuropathy in a large series of patients who had paresthesias elicited. Other factors, such as needle bevel and type, physician experience, and technique may be more important than the eliciting of paresthesias *per se.* Also, as Selander[2] has pointed out, other etiologic factors, such as surgery, casting, tourniquet, and perioperative positioning, should not be overlooked when evaluating a postanesthetic neuropathy.

Next, Selander[1] dismisses the issue of the unpredictability of single-injection techniques of axillary block, based on Partridge's[4] cadaver study. The relevant question for clinicians is "Can one predictably block all of the major nerves of the brachial plexus through the single injection block technique?" Clinically relevant studies[5–7] indicate that the single-injection technique cannot predictably block the radial and musculocutaneous nerves. We agree with Vester-Andersen that investigations intending to evaluate the influence of single factors on the quality of blockade should require thorough testing of analgesia in all segments of the arm.[7] Merely listing "success rate" does not validate a technique.

* Winchell SW, Wolfe R: The incidence of neuropathy following upper extremity nerve blocks. Reg Anesth 10:12–15, 1985