reach its target. That complicates matters, as the cation's very charge virtually imprisons it when diffusion barriers block the way. The task of diffusion falls to the lipid-soluble neutral base, which carries the local anesthetic molecule through the membrane. In short: the cation is the molecular species that plugs the channel, but the molecule must first be in the base form to get there.

Certain channel-blocking marine toxins (tetrodotoxin, for instance) circumvent this handicap in that they bind to receptors located near the entrance to the sodium channel, where it faces the extraneural environment. Derivatives of these drugs thus may well turn into useful blocking agents, since they do not have to rely on transmembrane diffusion to reach the internal action locus—as conventional local anesthetics must do.

Finally, a few words about "use-dependent inhibition," a topic detailed at some length in the review article. While intensity of (and recovery from) experimental blockade may be varied to some extent by manipulating the frequency of stimulation, the phenomenon's clinical relevance remains to be seen.

With the landmarks now well in sight, the reader can all the better savor the technical niceties and experimental subtleties of Strichartz's polished review article.

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Control of Respiration

OBESITY AND RESPIRATORY DRIVE In some markedly obese patients, respiratory response to carbon dioxide is significantly decreased. Can this abnormality be reversed by dietary manipulation? The authors have studied 18 obese patients (six with the obesity–hypoventilation syndrome and 12 with normal CO_2 responses). Pulmonary function, blood gases, serum ketone levels, and ventilatory response to CO_2 were evaluated at three times: 1) Control period of 3–5 days during which patients were maintained on a 2,500-kcal diet (40 per cent carbohydrate, 40 per cent fat, 20 per cent protein); 2) Ketosis was induced for 3–7 weeks by fasting (13 subjects) or a 400-kcal diet of protein (five subjects); 3) Patients were re-fed with a 1,000–1,200-kcal diet for 7–10 days. Studies were performed at the end of each phase. Changes in weight were similar in the hypoventilating and control groups. CO_2 sensitivity was unaltered by ketosis in the obese controls. However, in the hypoventilating group, CO_2 response was more than doubled in the ketotic phase (0.8 ± 0.1, 1.8 ± 0.2, 0.9 ± 0.1 l/min/torr in the three phases). This improvement could not be related to changing weight, pulmonary function, arterial blood *p*H, or differences in ketosis between the two groups. There was a significant relationship between CO_2 response and ketone-body concentration in the hypoventilating subjects. The authors conclude that the decreased ventilatory response to CO_2 occurring in some obese patients may be returned toward normal by dietary manipulation. (*Fried PI, and others: Effect of ketosis on respiratory sensitivity to carbon dioxide in obesity. N Engl J Med 294: 1081–1086, 1976.*)