reduction of the contractions induced in the stomach preparation. This supports the results of one further separate experiment on longitudinal stomach strips where imolamine (10 μg/ml) did not alter the acetylcholine dose-response curve but butalamine (10 μg/ml) caused a shift to the right and a flattening of the curve.

From these preliminary experiments, it would appear that butalamine is a more effective smooth muscle relaxant compound than imolamine. It has a similar potency to aminophylline on isolated human smooth muscle. Imolamine has a variable action on tone, producing an increase in ileum and uterus and a decrease in stomach.

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Protection against *m*-fluorotyrosine convulsions and lethality in mice exposed to hypobaric hypoxia

Acute exposure to hypoxia shifts brain metabolism to anaerobic pathways (Gurdjian, Webster & Stone, 1949) and elevates γ-aminobutyric acid (Wood, Watson & Ducker, 1968). Drugs which cause convulsions and impair aerobic metabolism or deplete brain γ-aminobutyric acid should therefore induce fewer convulsions during hypoxia.

Semicarbazide is thought to act in this way (Killam & Bain, 1957) and the convulsions it induced were antagonized by hypobaric hypoxia (Baumel, Shatz & others, 1969). *m*-Fluorotyrosine impairs oxidative metabolism in brain (Weissman & Koe, 1967), and we now show acute hypoxia to antagonize the convulsions and mortality it produces.

Swiss albino, random-bred male mice (Charles River Farms), 22–26 g were housed at 21–23° with room lights alternating on a 12-h light-dark cycle. The hypobaric chambers (Baumel, Robinson & Blatt, 1967) were plexiglass desiccators (internal diameter 10 in, height 14 in) connected, in parallel, to a vacuum pump through a manifold which exhausted room air.

Drug solutions were freshly prepared immediately before intraperitoneal injection. The animals were injected and immediately placed, in pairs, in the four altitude-chambers which were then decompressed over a 10-min period to 364 mm Hg (10% O_2). Controls were placed in identical chambers open to room air (760 mm Hg, 21% O_2).

Hypobaric hypoxia protected against *m*-fluorotyrosine convulsions at 3 and 4 h after administration of the drug. Lethality was decreased throughout the exposure period (Fig. 1).

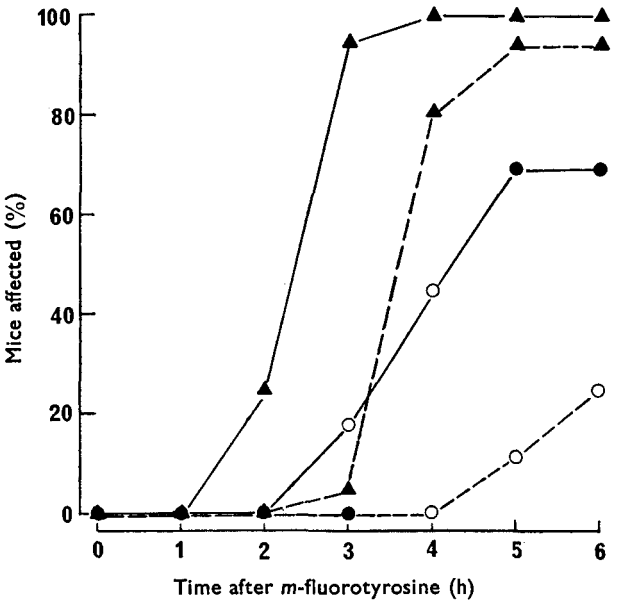

FIG. 1. Effect of hypobaric hypoxia on *m*-fluorotyrosine (10 mg/kg intraperitoneally) convulsions (—) and lethality (- - -). ▲ Sea level. ● Hypobaric. Clear circles denote significant difference ($P < 0.005$) from sea level.

The similarity of the acute effects of *m*-fluorotyrosine to those of fluoroacetate in several species (Chenoweth, 1949; Pattison, 1959) and accumulation of citric acid in brain and kidney of mice (Weissman & Koe, 1967) suggests that metabolism to fluoroacetate and blockade of the Krebs cycle by this metabolic poison is the mechanism of convulsions produced by *m*-fluorotyrosine. Hypoxia may antagonize *m*-fluorotyrosine convulsions by one or more of three probable mechanisms: hypoxia may decrease the rate of conversion of *m*-fluorotyrosine to fluoroacetate; increased dependence of neurons on anaerobic metabolism during hypoxia may reduce the consequences of impairing aerobic metabolism by fluoroacetate, or a rise in brain γ-aminobutryic acid during hypoxia (Wood, Watson & Ducker, 1968) may increase the threshold of vulnerable neurons to seizure activity.

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