while the rapidly growing carcinoma had a much lower content than normal. This suggests that the growth in the nonmalignant epidermis may be associated with the ability of the cells to increase the intracellular concentrations of the amino acids necessary for protein synthesis, whereas in the malignant tumor the mechanisms for protein synthesis are much more efficient and can operate at a greatly accelerated rate, even in the presence of smaller concentrations of amino acids.

Several aspects of this work are being studied further.

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Blocking Action of Tetraethylammonium on Axon Reflexes in the Human Skin

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Tetraethylammonium (*4*), which is now enjoying a wide trial as a diagnostic and therapeutic agent, is believed to exert its effects by the specific blockade of autonomic ganglia (*1, 2*). It is of interest, therefore, that in connection with some studies of the autonomic pharmacology of the skin we have obtained evidence that tetraethylammonium may exert an action on peripheral nerve fibers.

In most individuals the intracutaneous injection of acetylcholine in appropriate concentrations induces pilomotion and sweating, which occur very promptly after injection of the drug and extend for a considerable distance from the site of injection. These responses have been shown to be due to axon reflexes dependent on the integrity of the postganglionic sympathetic fibers (*5*).

By previously infiltrating the skin with tetraethylammonium we have been able to inhibit the axon reflexes of pilomotion and sweating induced by acetylcholine.

Pilomotion was elicited by the intracutaneous injection of 0.1 ml of acetylcholine hydrobromide, 1: 25,000; axon reflex sweating, by the injection of 0.1 ml of acetylcholine hydrobromide, 1: 500. Sweating was demonstrated by the ferric chloride–tannic acid method of Silverman and Powell (*6*). Axon sweating must be distinguished from the local response, which is confined to the area of the wheal, and from the sweating which follows the lymphatic diffusion of acetylcholine. Areas of the volar aspects of both forearms were selected for each test. The control area was prepared by the intracutaneous injection of 0.1 ml of physiological saline. The corresponding contralateral area was prepared by the intracutaneous injection of 0.1 ml of tetraethylammonium chloride, 1: 100.

It should be noted that tetraethylammonium itself, in the range of 1:10 to 1: 100,000, does not induce pilomotion or sweating.

In 15 experiments on 7 subjects in no instance did pilomotion occur when acetylcholine was injected into the spot where tetraethylammonium had been injected 1–2 min previously. Injection of acetylcholine into the control area treated with saline in every test produced typical pilomotion over an area of 2–3 cm in diameter surrounding the injection site and lasting for 45–90 sec. In 12 experiments on 8 subjects axon reflex sweating was either completely inhibited or markedly suppressed when acetylcholine was injected into the spot where tetraethylammonium had been injected 1–2 min previously. The local sweat response was not impaired. Injection of acetylcholine into the control area treated with saline in every instance produced typical axon sweating over an area of 2–4 cm in diameter.

Since these axon reflexes of the skin depend on the integrity of the postganglionic sympathetic axon and since they are blocked by the presence of tetraethylammonium locally in the skin, it is presumed that the blockade occurs along the course of the efferent sympathetic fibers in the skin.

The only other theoretically possible site of the stimulating action of acetylcholine and the blocking action of tetraethylammonium is the neuro-effector junction. In any case, there are no ganglion cells in the skin, although these axon reflexes occurring over the peripheral neural apparatus behave pharmacologically as though the site of stimulation were an autonomic ganglion. Rothman and Coon (*5*) pointed out this similarity and demonstrated that, as in the autonomic ganglia, nicotine or α-lobeline could be substituted for acetylcholine as the stimulus. The present study reveals a further similarity, namely, the blocking by tetraethylammonium of the nicotinic stimulating action of acetylcholine.

Evidence of the specificity of this blocking effect is the fact that we have been unable to inhibit with tetraethylammonium the flare which surrounds histamine-induced wheals of the skin, an axon reflex which is dependent on the integrity of afferent fibers of the skin (*3*).

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