CONTROL AND MIXIMIZATION OF TOBACCO SMOKE
DOSE IN CHRONIC ANIMAL STUDIES

Why do we need inhalation studies with whole tobacco smoke, and what can we hope to accomplish with them? A stated purpose of the tobacco and health program is to develop a less hazardous cigarette (Reference 1). The major risks associated with tobacco smoke are cancer, notably respiratory tract cancer, chronic respiratory disease(s), and cardiovascular disease(s). While the toxicity and the harmful effects of individual tobacco smoke components can be assessed in bioassay systems not involving inhalation exposure, the full pathogenic potency of as complex a mixture as tobacco smoke ultimately must be determined by inhalation studies with whole smoke. This presentation focuses on some crucial problems related to dosimetry and maximization of smoke exposure in tobacco smoke inhalation studies. We will limit our discussion to efforts aimed at the improvement and development of bioassays for testing the chronic toxicity and carcinogenicity of whole tobacco smoke in small laboratory rodents using passive smoke inhalation techniques.

Methods to Estimate Sustained Dose

Before discussing how to control and maximize the dose of tobacco smoke delivered to experimental animals, we need to take stock briefly of the major methods currently used to measure sustained dose and to suggest possible new approaches. It is important to remember that we will be measuring tobacco smoke components only, rather than whole tobacco smoke, but hopefully such measurements will be indicative of a class of compounds or a significant fraction of tobacco smoke. Currently, two main options are available for measuring or estimating tobacco smoke dose, with perhaps a third one to be added in the future. The first is to measure normally occurring tobacco smoke constituents (or their derivatives) in the body or body fluids of exposed animals. The simplest and most common example of this approach is determination of COHb. The second principal approach, developed more recently, is to label tobacco with chemical or radioactive tracers, then determine the amount of tracer in the respiratory tract of the exposed animals. This method is much more complicated than the former and requires that one have some knowledge of the fate of the tracer during pyrolysis, its distribution in the tobacco smoke, its volatility, etc. Typical examples of this approach are studies with decachlorobiphenyl (2), ^{14}C hexadecane (3), and ^{14}C-dotriacontane (4,5). The advantage of this method is that one can measure dose to the lung directly (though it may be debatable what fraction of tobacco smoke the measured quantity represents). The disadvantage is that (at least with the markers currently in use) a destructive test is required to determine the amount of tracer in the lungs. A third possible alternative is to use depletion of smoke components from the exposure chamber as a measure of uptake or dose to the animals. (This approach, if feasible, probably will apply only to static rather than dynamic exposure conditions.)

Label: *Report*
Also: *Scientific*

January 6, 1961

THE EFFECT OF TREATED AND UNTREATED CIGARETTE SMOKE
ON FROG CILIA[1]

The effects of cigarette smoke from OLD GOLD STRAIGHTS and from cigarettes made of treated OLD GOLD STRAIGHT tobacco were observed as described below.

The esophagus of a frog was removed, slit longitudinally and held flat on a small piece of cork by short pins. The tissue was washed with Locke's solution[2] (buffer) and dusted with finely powdered carbon. The sample thus prepared was placed in the smaller portion of a lucite box consisting of two chambers. The small chamber is 5 x 5 x 2.5 cm. internally, while the larger chamber, which is connected to the smaller one by a glass tube, is 5 x 5 x 5 cm. in size. Both chambers have removable airtight covers, and the side of each is fitted with a No. 8 hypodermic needle extending into the chamber. The top of the larger chamber is fitted with a cigarette holder, which opens into the chamber just above the edge of a perforated baffle, set at 45 degrees to the horizontal and extending to the bottom corner of the chamber. The purpose of this baffle is to mix the smoke as it is drawn into the chamber with the air already present.

A lighted cigarette was placed in the holder. The rate of transport of the carbon particles by the cilia was observed under 40 X magnification before application of smoke. This value was used as control. By means of a 30 cc. hypodermic syringe, several 30 cc. puffs of smoke were drawn into the larger chamber. Then, by means of the same syringe, one 30 cc. sample of the diluted smoke was drawn through the connecting glass tube into the smaller chamber containing the ciliated tissue. The entry tube was so placed that the entering stream of diluted smoke was directed immediately onto the tissue.

Label: *Scientific*
Also: *Report*