

EFFECTS OF TOBACCO SMOKE UPON MICE

ARTHUR T. JANECKE AND KENNETH S. FITZGERALD

Loyola University, Chicago, Illinois

*Bogen*¹ states that under ordinary conditions many competent observers have failed to note any deleterious effects from the use of cigarettes. Also from our own general observations it would appear that moderate cigarette smoking has no bad effect in normally healthy women. However, because some women realize that it is a mother's *duty* to bear her child not only alive, but also healthy, and because smoking may have a harmful effect upon the course of pregnancy, a popular question has arisen: "What are the effects of cigarette smoking in a pregnant woman?"

Viewpoints by laymen and members of the medical profession on the numerous questions involved are decided, but yet conflicting, and are unsupported by experimental or statistical data. Upon reviewing the literature of the relatively few experiments performed in an effort to answer these questions we encountered many limitations: Primarily, the number of studies on this subject is relatively small. Secondly, the findings of the various authors are too contradictory to permit the drawing of reliable conclusions. Finally, in too many instances, the number of animals used in the experiments were too small to gain convincing results.

After considering all these facts the only conclusion we can possibly reach is that the tobacco problem has not been studied sufficiently, and that it may prove more serious than is generally recognized.

In most of the experiments that were performed to determine the effects of tobacco smoking, injections of pure nicotine were used. It was not intended that the effects of injected nicotine be considered the same as those of smoking, but because nicotine is the most potent poison in the tobacco leaf, it was for this reason that nicotine alone was studied. A summary of some of the results obtained by this method is as follows:

*Hatcher & Crosby*² have demonstrated that lactating mothers secrete a sufficient amount of nicotine into their milk to cause a severe case of nicotine poisoning in their offspring.

*Edmunds*³ reports that young animals were more susceptible to nicotine than older ones. This susceptibility resulted in most cases in death even after very mild doses.

*Allen, Behrend, & Thienes*⁴ have found that while "control" animals showed an abundance of subcutaneous and intraperitoneal adipose tissue, the nicotine injected

COMPARATIVE SMOKING DATA OF MAN AND OF MOUSE

MOUSE LIFE IS A SPEED UP
OF HUMAN LIFE

TEN DAYS IN THE LIFE
of a MOUSE IS EQUAL to
about a YEAR IN A MAN'S...

MAN	MOUSE
365 days	10 days
365 days	1 days
876 hrs.	24 hrs.
52,560 Min	1,440 Min
52,560	= 1,440
* * 75	X
52,560 X = 108,000	
X =	2.054 MINUTES

* BY OBSERVATION WE HAVE NOTED THAT WHEN A HUMAN BEING SMOKES A CIGARETTE, TOBACCO SMOKE IS IN THE LUNGS FOR ABOUT THREE MINUTES PER CIGARETTE MAKING THE SMOKING OF A MOUSE EQUIVALENT TO A HUMAN'S SMOKING 25 CIGARETTES PER DAY, WE HAVE = $25 \times 3 = *75$

animals showed only a scanty amount of it. "Controls" of both sexes had as much as two times the amount of fat as did the nicotine injected animals. However, Dixon & Lee⁵ because of experiments carried on at the University of Minnesota were opposed to the idea that nicotine had any effect upon the weight of the animals.

According to Hazel E. Fields⁶ of Occidental College, California, who used the "smoking" technique exclusively, it was learned that experimental animals weigh less on a greater food intake, and that tobacco smoke apparently did not decrease skeletal growth in young animals fed with an adequate diet. The adrenal glands of the smoked animals showed a very noticeable increase in weight probably due to hypertrophy resulting from the oft-repeated, slow absorption of nicotine in minute amounts from the musoca of the mouth and respiratory tract. Also, Miss Fields states that it is extremely unlikely that continued stimulation of adrenal medulla and cortex would not

exert a considerable influence upon at least the pituitary and gonad.

Perhaps the most conclusive results thus far obtained in work on pregnant animals were obtained by Dr. Essenburg⁷ of Loyola University Medical School, Chicago. When performing his experiment he used at least seven times as many more animals as did any of the previously mentioned experimenters. He used not only the nicotine injection technique, but also a smoking technique, after which our experiments were patterned. He noted that:

Two thirds of all the young of treated mothers were underweight; the young from the nicotine-injected mothers being more underweight than those from the smoked mothers. This underweight group remained underweight during the entire period of observation, and many were not only underweight, but also died early.

Of the females injected, 63.3% lost one or more young before weaning, and 33.3% lost all of their young.

Of the mothers exposed to tobacco smoke 28% lost one or more of their young before weaning, and 13.5% lost all of their young.

Of the mothers smoked prior to mating but not during pregnancy, 23.3% lost one or more of their young before weaning, and 25% were underweight. In both groups of the treated mothers, temporary sterility, resorption of young in utero, and abortions were noted.

Dr. Gerd Umbehaun, an eminent German physician, by way of observation in his many years of practice had noted that women who smoke have lessened secondary sexual characteristics.

At Loyola University, Chicago, we are endeavoring by experiment to observe the effects of cigarette smoke on mice. We had chosen mice primarily because they were very readily available and because of their rapid reproduction and development. Our experiments are planned to:

1. Observe the effects of cigarette smoke on female mice from the time that they become independent of the parent, through their developing stages to adulthood, during pregnancy, and the consequent effect on their offspring.

2. Observe the effects of cigarette smoke on male mice from the time that they become independent of the parent, through their developing stages to adulthood, noting especially their fertilizing ability and sexual instincts while being treated.

3. Although the above mentioned two are our primary interests, certain other observations incidental to the experiment have been, and will be recorded.

Some of the observations made during the short period of time this experiment has been in progress, agree in part with the observations made by experimenters using the nicotine-injection technique. Before stating some of our observations, those resulting from the nicotine-injection technique are: excitations or convulsions, dyspnea accompanied by gnashing teeth, stiffening of the hind legs and tail, and other general reactions indicating a reduced threshold of irritability.

Regarding our experiment, the mice when in the smoking chamber were in general quiescent, seeming to avoid deep respiration by decreased activity. Only on a few occasions, toward the latter part of the smoking period, were the mice seen

to make an effort to get out of the smoking chamber. For the first few smokings the animals were known to have slight nasal inflammation and teary eyes, especially because the smoke was especially irritating. Although the stools were of the same general appearance and there was no outward evidence of gastro-intestinal disturbances increased defecation occurred, but gradually decreased as the animal became more accustomed to the smoke. Sexual interest and instinct does not express itself during the smoking and immediately following the smoking. A seemingly painful breathing, accompanied by slight wheezing noises, becomes noticeable toward the end of a smoking. Contrary to the results obtained by Miss Fields of Occidental College, California, who noted that both qualitatively and quantitatively the smoked animals were more active for a period of 15 minutes to 1½ hours following a smoking, we have noticed that the smoked mice remain exceedingly inactive during the period immediately following the smoking. During this period, sexual interest is lacking, and the desire for food, in spite of their hunger, is lacking. Throughout this entire period the mouse lies on its ventral surface, breathing at a normal rate, but showing a very reduced threshold of irritability.

Up to date three rather unique reactions were given by three experimental animals—two females, one of which was pregnant at the time, and one male. After 10 and 9 smokings respectively, the animals fell into a state of convulsion lasting from 2 to 5 minutes, during the early part of which there was no reaction to stimuli, and a temporary paralysis of the entire pelvic region took place. During the recovery period, as the animals made an effort to walk, progress was made in a lateral rather than a forward direction due to the position of the hind limbs clasped in paralysis.

While it can always be said that results obtained upon one animal form cannot be transferred to another, nevertheless definite results obtained in the mouse have a very high probability of holding true in some degree for man. By means of a system devised by my colleague, Kenneth Fitzgerald, we have determined the length of time a mouse would have to be subjected to smoke in order to bring about effects which would be equivalent

to effects produced in a human who smokes twenty-five cigarettes a day. See figure 1.

The moist surfaces, such as the hair under the mouth which frequently become wet with saliva, tend to collect the particles in the smoke. The mice ingest these substances in their vigorous cleaning processes following the smokings. Therefore, we may say that the animals may actually swallow as much of the material as does the human smoker when his mouth is in contact with the pipe or the cigarette. However, again we have absolutely no quantitative means of comparison here.

You may wonder whether our dosage and mechanical smoking technique adequately imitates human's smokings. Although this is a debatable question the factors involved justify our making an analogy between mice and men. In ending, may we once again emphasize the

fact that we realize the results obtained on mice cannot be transferred *directly* to the human, but the essential results obtained will challenge our own reconsideration of the problem.

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