

Discussion with Dr. M.H. Scovors, Ann Arbor, Michigan
1st October, 1964.

PSG 7
B 1190

Present: P.J.R.
G.F.T.

A.M.A. Research into Smoking and Health

To date, the Committee (of which Scovors is Chairman) appointed by the Education and Research Foundation of the A.M.A. to direct the programme for using the \$10,000,000 fund contributed by the U.S. cigarette manufacturers, has approved 28 grants. The total cost of these over the periods for which they have been approved will be \$2,400,000. Details of the grants are attached.

The main considerations which have been in the minds of the Scovors Committee in making these grants have been:

- (1) It is necessary to get more good people to undertake research in the smoking and health field, whether or not they live in U.S.A.
- (2) Research into cancer is not excluded but it has been over-supported in relation to other aspects. Under-supported have been research into respiratory disease, cardiovascular disease, cellular studies, ciliary activity, pharmacological and psychological reasons for smoking.
- (3) It is particularly necessary to find means of determining nicotine in the blood and organising a supply of radio-active nicotine. The Committee aim particularly at developing techniques.
- (4) The Committee do not plan to build their own laboratory though they may use the general medical research laboratory being built for the E.R.F. of A.M.A. in Chicago.
- (5) Where gaps exist, the Committee will initiate research projects to close them. They already have 2 or 3 such projects.

- (6) The Committee is not concerned with modifications to cigarettes, how to treat tobacco etc. The manufacturers are more competent to do this. Similarly, the Committee is not concerned with cigarette tars, which would require a laboratory for their production.
- (7) The House of Delegates of the A.M.A., in accepting the fund, looked to it being used for the development of safe cigarettes. The Committee considered that they were not set up to do this, and had no manufacturing competence, etc - Soevers said they had a hard time getting away from this objective.
- (8) The Committee would support epidemiological studies if they received good applications.
- (9) The Committee may support research in more fields as they get more and more projects going.
- (10) They may add other experts (e.g. pathologists) to the Committee; just feeling their way at present.
- (11) If they find good projects, they won't hesitate to spend over the \$10,000,000 as the A.M.A. would have no difficulty in finding more money.
- (12) They have refused to finance anti-smoking clinics or education.
- (13) They expect to co-operate closely with CTR.

The projects approved to date include:-

- (a) McKennis working in Richmond with Larson to produce radio-active nicotine for Schmiterlow.
- (b) McKennis may also be able to find a method for determining nicotine in the blood.
- (c) Lemaire of University of Texas is doing detailed study of different types of cough. Soevers thought more work was required in this field.
- (d) A study of the psychological characteristics of smokers.

SeEVERS' Personal Views

1. SeEVERS does not believe that it has been proved that smoking causes lung cancer. There is an association and it should be made known. The strongest evidence for a causal connection is Auerbach's work, but it is not conclusive. SeEVERS is not sure the validity of the statistics.
2. SeEVERS is convinced the main reason why people smoke is the nicotine. He thinks it important to keep the nicotine content up. He has suggested to Hanover of the American Tobacco Co. that they should add back nicotine to the cut tobacco and then reduce both nicotine and tar, as in Carlton, by filter and porous paper. To produce a non-tobacco cigarette was contrary to common sense.
3. SeEVERS considered that the chronic toxicity of nicotine must be low. There was only negative evidence to support his view, he said, but if prolonged intake of nicotine was harmful, it would have caused very much more trouble than it had.
4. He thought that nicotine had both a stimulant effect (when taken in small doses) and a depressant effect (in large doses)
5. He thought the effect of nicotine might vary with the method of smoking. Deep inhaling might give sudden large additions of nicotine to the blood; non-inhalers might keep a less fluctuating level of nicotine in their blood.
6. Nicotine affected both the autonomic nervous system (see Langley's work) and the central nervous system. He thought Burn was probably right in his conclusion that nicotine stimulated the adrenals and released catecholamines but thought this effect might not be important with the dose levels obtained in smoking.
7. He thought nicotine (and smoking) could do no harm to the healthy heart. On the other hand, it was only good medical practice for a man with an unhealthy heart not to smoke.

SeEVERS' Own Research

SeEVERS runs a laboratory on addiction as an adjunct to the Federal Narcotics Bureau at Lexington, Ky. He believes that monkeys and man like and dislike the same drugs, and he therefore has a colony of 210 monkeys, which we saw. He also uses dogs, which we did not see. We met Dr. Denoau (in charge of the monkeys) and Dr. Yanagita (in charge of

the addiction experiments).

(a) Addiction experiments

We saw 24 monkeys fitted with metal frames attached to a moveable arm, anchored to the back of the cage. A polyethylene tube passed through this arm into the animal's jugular vein and its heart. The other end of the tube was attached outside the cage to an electronic control. The control mechanism could be operated in two ways -

- (a) It shot a measured amount of a drug into the heart at specified or random intervals.
- (b) The animal could press a bar in its cage to give itself a shot of the drug. Either one press could deliver a shot (as of nicotine base) or it had to press the bar 2000 times to get one shot (cocaine) or even 10,000 times (codine). If it was necessary to tempt the animal to press the bar, a raisin would be put on it. If it was desired to penalise the animal for pressing the bar, it received a blast of air.

The animals on nicotine were started on a fixed dose and frequency cycle with 25 micrograms of nicotine 40 times a day. They now received 600 micrograms 4 times a day. This dose appeared to give some respiratory stimulation. When put on self-controlled dosage, they liked to administer to themselves morphine, alcohol and nicotine base. They would not press the bar when what they got was chlorpromazine or saline. When given barbiturates, they would press the bar until they knocked themselves out. When they recovered, they started the same procedure again. When given alcohol, they went on until they knocked themselves out, but on recovering did not repeat the dose.

Some animals had electrodes inserted in their brains to enable an electric stimulant to be given to them.

(b) Nicotine chronic toxicity tests.

Monkeys were also given injections of nicotine in their backs to see what the chronic toxic effects were. It was fascinating to see the monkeys come flying out of their cages to receive injections. They always came in the same order, apparently without reluctance, though they cowered in a corner and hid their faces on being injected.

*Copy in Medical
Symptoms*

Immediately it was over, they sprang back into their cage in the same order.

The dosage had been worked up to the very high daily rate of 13 mg/kg. As the monkey weighed 4 to 4.8 kg, this was equivalent to a daily dose of about 60 mg nicotine. At this dosage there was some abscessing suggesting that some of the nicotine was not being absorbed.

(c) Human experiments

Seevers was planning to carry out experiments on volunteers in which a radio-active device would inject nicotine at unknown random intervals into a vein through a polyethylene catheter. It was proposed to observe -

- (i) the effect of this on non-smokers
- (ii) the effect on the desire of a smoker to smoke -
o.g. would heavy smokers smoke less?

Surgeon General's Advisory Committee

Seevers said that it was a Committee of prima donnas. Though none of the members had publicly expressed views on smoking and health they all had very definite views. The Surgeon General never came near the Committee. Handloy acted as Chairman of meetings; he was pleasant but ineffective, allowing far too much irrelevant chat. Baynes-Jones, as oldest member, had to step in from time to time to get points settled. Two whole days were spent discussing the meaning of "cause". The political people tried to hurry up the Committee but did not otherwise try to influence them. The "members responsible for cancer" (probably Kurth) submitted a draft for the chapter on cancer that had been written by the American Cancer Society. This was thrown out.

Handloy for
behavioral studies

Should we start
go + see Seevers

ACA wants to do
more work first

his action
yet
only just starting

allies to
Clark,
Stern
Hill
norm of
behavior

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