

Introduction

Jack E Henningfield

It gives me great pleasure and pride to introduce our concluding speaker, Dr Charles Robert Schuster. Dr Schuster was appointed Director of the National Institute on Drug Abuse (NIDA) in 1986, and he resigned voluntarily, as a birthday present to himself, in 1992. He is now a scientist, mentor, guru, ad hoc guidance counsellor and everything else with us at the Addiction Research Center, and I can't tell you what a pleasure it is to have him there.

Yesterday Frank Vocci said this field is working; we've come a long way from people quitting on their own at 2% annually. And the field has been working, in part, because of the efforts of Bob Schuster. He did the pivotal study in the 1960s that demonstrated the viability of nicotine replacement, one of the most widely cited studies in the basic litera-

ture. His service on numerous committees of the Institute of Medicine, National Academy of Sciences and World Health Organisation have laid the groundwork for the criteria for evaluating addictions, and for evaluating medications.

And finally, as director of NIDA, I can tell you he was there at a time that the White House was anything but sympathetic to nicotine research, and he fought an uphill battle to sustain funding for nicotine research at the ARC, and in the extramural programmes. Perhaps his most truly courageous day was when Ron Davis and I met with him to discuss what would become of the addiction report because we knew it would have little credibility if NIDA would not back it in every way, and Bob Schuster, with unwavering support, backed and supported it.

Research issues in smoking cessation

Charles R Schuster

It was mentioned by Jack Henningfield that my career in tobacco research, which was very short-lived, occurred in the 1960s. To start, I would like to review some of my early pharmacological research on cigarette smoking behaviour.

During the 1960s, it was not clear that cigarettes acted as a delivery device for the psychoactive substance nicotine. Rather, psychoanalytic theories of the aetiological basis of cigarette use stressed oral gratification. In order to look more closely at the pharmacological effect of nicotine on humans, five human subjects (referred to then simply as 'smokers'), all of whom were dependent on tobacco, were recruited for a study supported by the American Medical Association (Lucchesi, Schuster and Emley, 1967).¹ Ben Lucchesi, a cardiovascular pharmacologist and physician, and I looked at what would happen over a 6-hour period to cigarette smoking frequency if smokers, who believed they were being studied for an unrelated purpose, were infused with nicotine.

Subjects were 21- to 30-year-old male and female volunteers. They were studied for 15 consecutive days, and completed a 6-hour

experimental session daily. A Y-adaptor was used to infuse intravenously 0.9% sodium chloride continuously, and either nicotine bitartrate or saline solution, randomly. The subjects were unaware, at all times, of the order of infusion. Both the number of cigarettes consumed during each session and the weight of the unsmoked portion of the cigarettes was measured and recorded. Only subjects who were capable of tolerating a 4 mg/h dose of nicotine without subjective responses were included in this study.

It was found that Subject 1 smoked 17.9 cigarettes on average across seven sessions in a 6-h period, with very little variance, and a standard deviation of only 0.72. The rest of the subjects showed the same type of regularity from session to session. As a matter of fact, Subject 2 smoked 7 cigarettes during every single one of the four sessions in which he received a saline infusion through an indwelling intravenous catheter.

When the subjects were infused with nicotine, at a rate of 2 mg in the first hour and 4 mg/h for the remaining 5 h of the 6-h session, we saw a statistically significant, and I think biologically significant, decline in all five of the