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Addiction to Smoking – Is there a Genetic Component?

Presented by:

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BACKGROUND [1]

Work by Peto and colleagues (as cited in Shafey, Dolwick, & Guindon, 2003) suggests that nearly **30%** of all deaths among adults aged 35–69 years in the United States can be attributed to the **persistent use** of cigarettes, including approximately

- **27%** of all cancer related deaths in women and
- **44%** in men.

[1] Meeting Report: Genetic research on complex behaviors: An examination of attempts to identify genes for smoking. *Nicotine & Tobacco Research* 9(8):883–901, August 2007.

Among those who smoke cigarettes, evidence suggests that beginning at age 40 years there is increasing loss of life depending on the age of quitting cigarettes, with as much as 10 years lost for those smoking cigarettes throughout their life (Doll & Hill, 2004).

At the same time, smoking cessation therapies have disappointing success rates.

From a public health perspective, the most important aspect of cigarette smoking is **smoking persistence**, that is, **which individuals become long term smokers**, among the many who are exposed to tobacco.

- Strong consistent evidence suggest that **genetic factors** account at least in part for individual differences in long-term persistent cigarette smoking.

How are early and later stages of cigarette smoking related?

- Even in societies with high rates of cigarette experimentation, not all experimenters become smokers.
- Not all respondents who report smoking regularly at some point in their lives report a history of nicotine dependence or withdrawal.
- In an Australian study, about 50% with a history of regular smoking reported repeated failure at quitting cigarettes.

The Genetics and Epigenetics of Substance Abuse: NIDA/NIAAA Satellite Symposium at the World Congress of Psychiatric Genetics

Omni Shoreham Hotel

September 9, 2011 2500 Calvert Street NW, Washington, DC 20008

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

NIAAA National Institute on Alcohol Abuse and Alcoholism

NATIONAL INSTITUTES OF HEALTH

NIDA/NIAAA Conference

At that conference, 3 of the key talks were:

- **Genetics of Nicotine Addiction**
  Laura Bierut, M.D.
  Washington University in St. Louis

- **Genetics of Alcoholism**
  Howard Edenberg, Ph.D.
  Indiana University

- **The Future is Bright: Charting a Course for Genomic Medicine**
  Eric Green, M.D., Ph.D
  Director, National Human Genome Research Institute

A brief summary of the evolving data:

Addiction

- If a substance is never tried, there will never be addiction.
- There is tremendous variation in the addiction potential of various substances plus there is individual variation in the propensity to addiction in general and addiction to various substances, and these are slowly being teased apart

- The best, and sometimes perhaps the only, chance to avoid addiction among those with
  - Genetic predisposition, or
  - Strong social influences

  to nicotine addiction may be to avoid that first cigarette

Evolving Genetic Findings

- Specific genes have been linked to some patterns or metabolic pathways
- For most of these, the biologic mechanisms of the genes are not yet understood
- Some have been linked with metabolism, such as with the rapidity of metabolism of alcohol, and this may help explain some racial/ethnic differences in alcohol tolerance (E.g., Japanese vs. Irish)

Evolving Genetic Findings - **Alcohol**

- "Social" drinking in the teens so far has NOT been associated with any genetic predisposition NOR to alcoholism
- In contrast, a gene related to a predisposition to alcoholism seems to first "kick in" during the mid-20's and later
- *Reminder*: alcoholism is associated with increased morbidity and mortality from many chronic illnesses, including liver cancer

Nicotine

- A key addictive component in tobacco is NICOTINE
- If the nicotine content in a cigarette is **reduced**, smoking may **increase** to compensate in order to get the same dose
- As just discussed by Mr. Lee, nicotine has many physiologic effects as do the multitude of other chemicals in tobacco and in tobacco smoke

Nicotine

- For decades, the tobacco industry hid data and tried to create a climate of doubt; in particular, read:
  - *Doubt is their product. How industry's assault on science threatens your health*. By David Michaels, 2007, Oxford University Press
  - *Merchants of Doubt*. By Naomi Oreskes & Erik M. Conway, 2010, Bloomsburg Press

Evolving Genetic Findings - **Nicotine**

- A gene has been found that is **associated with persistence of smoking behavior (i.e., ADDICTION)**.
- In contrast to alcohol, this gene **acts beginning in the teens.**
- Corollary: once exposed, for these people it has been extremely difficult to stop smoking.
- Thus, it is critical to PREVENT that first initiation exposure to nicotine.
- Our youth-based efforts are thus EXCEPTIONALLY important.

Caveats

- Most of these genetic tests are in their infancy, and none come close to being 100% predictive.
- These are complex behaviors; genetics can be part of the story, but likely only in some
- It also is beginning to help us understand that some **familial** patterns may be partly social (shared environment, etc) and partly genetic

The Future

- Genetic data is being accumulated at exponentially increasing rates and decreasing costs,
- The amount of data has so far been outstripping anyone's ability to interpret it
- The NIH will be spending billions of $$$ over the next decades in an attempt to help clinicians use these data on behalf of their patients