WHAT IF WE FOUND THE MAGIC BULLET?

_Ideological and ethical constraints on biological alcohol research and its application_

Key words: biomedical research, disease concept of alcoholism, abstinence goal, medications, liver transplants, patient compliance

Abstract. Funding for biomedical research on alcohol is justified in terms of the eventual development of pharmacotherapies for alcoholism treatment. Three medications have so far been approved: disulfiram, an aversive substance with a 50-year history, not much used now because of patient noncompliance; and naltrexone and acamprosate, which are now thought to be mildly effective. Ideological and practical limits on the development of medications include the focus on “alcoholism”, rather than on reducing the harm from heavy drinking, and the requirement of abstinence as a goal. These constraints have been argued to limit the effectiveness of naltrexone, and have diverted attention from such substances as propylthiouracil with promise to prevent liver deterioration, and from the success of liver transplantation in reducing alcohol-related deaths. Patient compliance will be a problem with any medication that deters drinking, or takes the pleasure out of it, particularly when the treatment is coerced, as much alcohol treatment is, formally or informally. In light of this analysis, it is hard to imagine a medication (other than another psychoactive substance) which would be both politically acceptable and effective. There is a need for ethical consideration prior to the advent of such future developments as a preventive vaccine interrupting the action of alcohol on the brain. Refocusing on biomedical means of reducing health harms from alcohol would be a useful path forward.

THE RISE OF BIOMEDICAL RESEARCH FUNDING, AND ITS JUSTIFICATION

These are heady days for biological research in the alcohol field, particularly in the U.S. In 2001, well over half of NIAAA’s research spending was in this category (Midanik, 2002). Nor is American investment in biological alcohol research limited to the federal government. The Gallo Center in the San Francisco area, originally funded with $6.5 million seed money from the cofounder of the world’s biggest wine company, received $143 million from the state of California for a 1998-2003 “Manhattan project” studying the biological causes and treatment of alcoholism (Harper, 2001).

There is no doubt that biomedical research has contributed new knowledge and understanding of the biological side of alcohol issues. But the justification for the
investment in research is not just in terms of improving the stock of human knowledge. The fundamental justification is in terms of a cure -- of medications or other physical interventions which will reduce problems of alcohol. “The goal posts are to have drugs that are in trials”, as Kirk Wilhelmsen, a laboratory director at the Gallo Center, put it concerning the Center’s goals for 2003. “I’m fully expecting ... to redefine alcoholism based on the underlying biological process and what it is about alcoholism that’s inherited. If there’s a gene that’s involved, there’s a molecule that’s involved, and a drug that can be developed for that” (Harper, 2001). At the outset of the steepest rise in NIAAA’s spending on neuroscience research, Enoch Gordis, its director, stated the rationale this way:

Developing effective pharmacotherapies for alcoholism treatment is a top priority of alcohol research. Doing so depends on neuroscientists’ continuing elucidation of how alcohol acts on the brain to produce the fundamental phenomena of alcoholism -- tolerance, withdrawal, impaired control over drinking, and craving -- and how these phenomena can be interrupted or controlled. (Gordis, 1996)

**MEDICATIONS FOR ALCOHOL PROBLEMS: THE CURRENT SITUATION**

In terms of medications for alcohol dependence, the cupboard presently is not quite bare, but it is not very full. Discussions of medications in current use for alcohol cases usually confine themselves to three: disulfiram (antabuse), naltrexone and acamprosate.

Disulfiram, which has been around for 50 years, is basically an aversive drug. By interfering with the process of metabolization of alcohol, it makes drinking uncomfortable and presumably something to be avoided. But the big problem with disulfiram is “patient compliance”: that alcoholic patients do not continue taking it regularly. To some extent, this can be overcome by implanting the disulfiram tablet under the patient’s skin. A comparative study of the cost-effectiveness of different treatments ranks “oral disulfiram” quite low in effectiveness, but “disulfiram implants” among the top four treatment modalities (Finney and Monahan, 1996). Chick (2001) comments that “this is seldom used now, partly because the active drug was often not detectable in blood after about 2 weeks”. However, recent news reports on a famous English ex-soccer player’s liver transplant noted that for more than a year prior to the operation he had had surgically implanted disulfiram tablets; his doctor reported that “he found the implant treatment that he has had a great help over the last year” (Wilson, 2002).

Naltrexone and acamprosate both came to fore as treatments for alcohol problems in the 1990s, with naltrexone promoted primarily by U.S. champions and acamprosate primarily by Europeans. By 1996, “the development of naltrexone in the United States and acamprosate in Europe” was being hailed as “an important convergence of neurosciences and clinical research” (Gordis, 1996).