Knowledge of Alcohol as a Teratogen

The knowledge that alcohol was harmful to embryos has been known for a long time, forgotten, and then recovered. Philip Pauly (1996), a historian of science, has documented how the effects of alcohol on reproduction, once a thriving research field, became "scientifically uninteresting."

His story starts in the first years of the 1900s, when C. R. Stockard, a student of T. H. Morgan, showed that certain ions (notably, magnesium) had teratogenic effects on fish development. But when Stockard joined the faculty of Cornell University Medical School, he realized that physicians had no interest in piscine teratogenesis. He was given no laboratory as long as confined his work to minnows. However, one of the senior physicians there, Dr. Alexander Lambert, was active in the treatment and prevention of alcoholism and had recently summarized the clinical evidence that alcohol produced idiocy and epilepsy in the children of alcoholics. In 1910, Stockard began to study the possible causes of these associations. Working on chickens and guinea pigs, he focused on demonstrating that parental exposure to alcohol could damage their offspring. (He could not get guinea pigs to drink alcohol, so he placed them in an airtight box containing alcohol-saturated cotton,

keeping them there until they showed signs of intoxication). The results were impressive. Matings of 14 "alcoholic" pairs produced three stillborn litters and only one live pup (who died shortly after birth). The nine control matings produced seventeen offspring with no early mortality. Matings of "alcoholic" males to normal females or *vice versa* also showed striking infertility and early mortality (Stockard, 1912a, b). Stockard believed the results were sufficient to "convincingly demonstrate the detrimental effects of alcohol on the parental germ cells and the developing offspring," and his research was greatly publicized in the reformist press, and was used in some of the most important speeches of the Temperance movement. The notion that male gametes were effected as well as female eggs was very much a part of Stockard's view. First, male drunkenness (not that of females) was seen as the big social issue, and either male or female gamete deterioration could "damage the race." Moreover, Oscar Hertwig and his two children had already shown that sea urchin or frog sperm produced defective embryos when exposed to radium. Publishing his new results in both zoological and medical journals, Stockard (1913a,b) reported that alcohol "weakened" both male and female germ cells.

In 1914, Stockard hired, as his assistant, the immigrant physician George Papanicolaou. (Papanicoulou's work on this project caused him to develop techniques for determining the estrous cycle of the guinea pig by sampling vaginal cells, a

procedure that ultimately became the "Pap smear.") Perhaps echoing *Exodus* 20: 5, Stockard and Papanicolaou's data (1916) suggested that the effect of alcohol treatment began "to fade out in the fourth generation." They argued that alcohol effected the cell's chromatin, and this would explain the differential fertility of alcoholic XX females and XY males. Alcohol was a toxic substance that caused reproductive failure and malformations.

At the same time, "hearty drinker and geneticist," Raymond Pearl, began his experiments on the effects of alcohol on chickens. He reported (1917) that his chickens exposed to ethanol laid fewer eggs, but that those eggs produced healthier offspring. In other words, alcohol was a beneficial selective agent. It eliminated the weak, allowing those who could take the assault to survive. He similarly reported studies showing that children of alcoholic parents were stronger than those born of sober backgrounds.

This began a scientific controversy over dosages, conditions, and the interpretation of data. Political and scientific leaders alike considered this controversy important, and new scientists began to work in this area. However, by 1919, all that changed. The American entry into World War I had interrupted the experimental programs, and the Prohibition Act of 1919 "solved" the drinking problem once and for all. The effect of alcohol on reproduction and development was no longer a pressing social issue. In addition, the tide was

turning due to the total "bone dry" prohibitions against alcohol. The population had gone from demanding limits on drinking to "resentment that the Volstead Act made even light alcoholic beverages hard for them to get. There was thus little incentive for culturally sophisticated researchers to do more to show that alcohol was deleterious" (Pauly, 1996).

Stockard changed roles completely, declaring that alcohol was, indeed—just as Pearl said it was—benefical for the race. At the Fifteenth International Congress against Alcoholism, Stockard (1920) scandalized his audience by saying, "Alcohol is one of the things that will tend to eliminate bad individuals, and inasmuch as from an economic viewpoint they may not do much good or amount to much, why not use this means to eradicate them? We can't look at this from an ethical or humanitarian standpoint; we've got to consider it on a scientific basis." (American science in the 1920s mirrored and reinforced the racist, classist, and anti-women biases of its constituents.)

A more profound reversal, and one that was to have profound importance, was that of Frank B. Hanson. Hanson was a Methodist minister who, in his late 20s, decided to pursue a new career in biology. Being a Methodist minister teaching zoology at a strongly pro-temperance university, he was probably interested in reinforcing the scientific basis for temperance, and he hoped to be more successful than Stockard in producing malformations in the

offspring of alcohol-exposed animals. He began experiments exposing rats to alcohol for a year as soon as they were weaned. The problem was that hardly any of his alcohol-treated females delivered any pups. So he cut down the exposure time. Under these conditions, they reproduced without any problem for nine generations. This change in experimental design changed the results and the interpretation. Now, Hanson saw ethanol as being neutral to health. Between 1923 and 1930, Hanson and his students published a series of papers in major journals contending that alcohol had no measurable effect on birth weight, litter size, mortality, sex ratio, learning, or even the tolerance for alcohol. He concluded that alcohol had no deleterious or beneficial effects on the progeny. There was nothing to look for. As Pauly (1996) says, "As a result the problem became uninteresting —that is, no meaningful issues remained to be taken up with the methods conceivable then or in the near future." Pauly hypothesizes that Hanson could view his work as being pro-Tolerance. Since both Stockard and Pearl were claiming the anti-Tolerance position that alcohol was beneficial, Hanson was providing scientific evidence against that view. Concerning reproduction, alcohol was neutral.

This was the view that prevailed. In 1939, when the Rockefeller Foundation was deciding which scientific initiatives should be funded, they concluded that no new research on alcohol was needed. Hanson was a member of the Rockefeller staff at that time, and

his voice was important in any discussion of alcohol related research. Moreover, the one big study on alcohol funded by the Rockefeller Foundation, Alcohol Explored (Haggard and Jellinek, 1942), concluded that "no acceptable evidence has ever been offered to show that acute alcoholic intoxication has any effect whatsoever on the human germ, or has any influence in altering heredity, or is the cause of any abnormality in the child." Pamphlets to expectant parents (such as the ones distributed by the Rutgers Center for Alcohol Studies in 1955) calmed parents' fears, stating that, "old notions about children of drunken parents being born defective can be cast aside." Research in this area had almost completely disappeared. According to Pauly, it was only in the 1970s that the interests of heavy drinkers (especially Native Americans), research-oriented physicians, and the political conflicts attending social transformations caused the reopening of alcohol research. In 1973, Jones and Smith were able to identify a fetal alcohol syndrome and initiate a new research program.

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