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ONE HUNDRED YEARS OF ALCOHOLISM: THE TWENTIETH CENTURY

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Abstract — The past 100 years witnessed the formation of a disease concept of alcoholism and a rapid increase in the knowledge of its aetiopathology and treatment options. In the first half of the century, public sanctions aimed at the abolition of alcoholism. In the United States, alcohol prohibition was revoked in the economic turmoil of the Great Depression. In Germany, proposed medical procedures to reduce the fertility of alcoholics had catastrophic consequences during the fascist dictatorship. A revived focus on alcoholics as patients with a right to medical treatment came out of self-organized groups, such as Alcoholics Anonymous. The current disease concept includes the psychosocial and neurobiological foundations and consequences of alcoholism. Neurobiological research points to the dispositional factor of monoaminergic dysfunction and indicates that neuroadaptation and sensitization may play a role in the maintenance of addictive behaviour. New treatment options include pharmacological approaches and indicate that behaviour and motivational therapy and the attendance of patient groups may equally reduce the relapse risk. The task of the future will be to apply scientific discoveries in the best interest of the patients and to support their efforts to be respected like subjects suffering from other diseases.

INTRODUCTION

Alcoholism research and treatment underwent significant changes in the 20th century. Within the last 100 years, a disease concept was formed, which is now widely accepted, the psychosocial and neurobiological consequences of alcoholism have been characterized and treatment programmes have been established and continuously refined. First attempts were made to formulate models of the disposition and development of alcohol dependence that integrate both neurobiological and psychosocial findings. In this essay, we will highlight some of the cornerstones of our present understanding of alcoholism and reflect on some of the organizations and research traditions whose activities were crucial in the development of current concepts. Given the scope of the subject, this review will be both incomplete and subjective, and we will be unable to mention many subjects and institutions whose contributions to current alcoholism concepts were as important and fundamental as the ones we are able to discuss.

THE HERITAGE OF THE 19TH CENTURY — A CONCEPT OF ADDICTION, TEMPERANCE AND DEGENERATION

An uncontrollable, overwhelming and irresistible desire to consume alcohol was described by Benjamin Rush in 1784, and delirium tremens was independently described by both Pearson and Sutton in 1813 (Kielhorn, 1988). Alcohol craving and withdrawal symptoms were integral parts of the concept of addiction and of the destructive effects of alcohol consumption promoted by the temperance movement in the 19th century (Levine, 1984). In several European countries and in the United States, temperance movements were stimulated by the excessive consumption of liquor and other highly distilled alcoholic beverages, which was uninhibited by cultural traditions and appeared especially problematic among poor working class families during industrialization (Levine, 1984; Henkel, 1998). There was, however, a fundamental difference to current concepts of alcoholism: the temperance movement suggested that anyone who consumed excessive amounts of alcohol would suffer from alcohol-related problems and did not suggest that alcoholism could affect certain specifically vulnerable individuals primarily (Levine, 1984; Heather, 1992).

A focus on the individual was promoted by degenerationism, the theory that biological factors, toxic environmental influences or moral vices may trigger a cascade of social, moral and medical problems, which increase in each generation and will finally lead to the extinction of that family (Bynum, 1984). The theory of degeneration was based on the pre-Darwinian concept that acquired character traits were passed on to the offspring and assumed that an array of different symptoms and diseases, such as impulsivity, alcoholism, strokes, dementia, microcephaly and epilepsy, were all expressions of one underlying pathology — degeneration (Hermle, 1986).

Degenerationism thus offered a medical explanation for the social problems which were so visible at the end of the 19th century, and excessive alcohol consumption played a crucial role in the concept, as it was seen as a vice which also affects the next generation. In the early 20th century, the degeneration theory suffered from an increasing knowledge about modes of transmission of heritable traits, which pointed to the separate inheritance of different mental and physical diseases, and distinguished between heritable traits and toxic effects on the germ plasm or embryo, thus fundamentally questioning the postulate of the inheritance of acquired traits (Hermle, 1986). However, degenerationism substantially contributed to the concerns about the specific alcohol-related problems of certain individuals.

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TRYING TO ERADICATE ALCOHOLISM — DIFFERENT APPROACHES

In the first 30 years of the 20th century, degenerationism and the successors of the temperance movement sparked widespread political activities in the field of alcohol addiction. In the United States, the Anti-Saloon League followed the approach of the temperance movement and focused on the general problems of alcohol consumption. It succeeded in the implementation of alcohol prohibition, which was legally enforced from 1919 to 1933. Prohibition was initially successful in reducing alcohol intake; however, illegal alcohol consumption slowly increased in the late 1920s (Tyrrell, 1997). Prohibition was finally abolished not so much because it failed to abolish alcohol intake, but because of shifting priorities in the Great Depression, when it was argued that liquor production would create jobs and that alcohol taxes might help to reduce income taxes (Levine, 1984).

In Germany, the focus on the individual and their heritable vulnerability to alcohol addiction was imbued with alarmist concerns about the proliferation of the mentally ill, which was supposed to threaten the survival of the nation or 'race.' Consequently, compulsory sterilization of 'severe alcoholics' was already advocated by some medical doctors before it was legalized during the Nazi dictatorship. The number of alcohol-dependent patients murdered during the Nazi regime is unknown (Henkel, 1998).

AFTER PROHIBITION — THE CREATION OF A MODERN DISEASE CONCEPT

It was in the wake of the failure of prohibition that the current concept of alcoholism was formed, and the worldwide shock about the cruelty and inhumanity of Nazi politics may have promoted the modern disease concept with its focus on individual therapy and its emphasis that alcohol addiction is a disease just like any other physical or mental malady (Levine, 1984; Henkel, 1998). A decisive point was the foundation of Alcoholics Anonymous (AA) in the late 1930s. Similar to previous temperance movements, Alcoholics Anonymous displayed a sympathetic and supporting attitude towards the addicted person, but unlike previous groups, AA was only for alcoholics and was not concerned with the general level of alcohol consumption in the population. In fact, the view that all it would take to create an alcohol addict would be his excessive alcohol consumption was no longer persuasive after the end of prohibition (Levine, 1984). Likewise, the existence of alcohol tolerance and withdrawal was widely neglected in the 1930s and early 1940s, although delirium tremens due to alcohol withdrawal had clearly been described by Hare 1910 in the *British Journal of Inebriety* (Edwards, 1990). Jellinek (1942) and the Yale Summer School on Alcohol Studies agreed with AA that alcoholism would be a disease with a progressive character and not a moral failing. The 1954 report of the World Health Organization (WHO) reflected this new focus on the individual and stated that 'the personal make-up is the determining factor, but the pharmacological action (of alcohol) plays a significant role' (Edwards, 1990). However, it was not until the mid-1950s that convulsions and delirium tremens regained public attention as symptoms of alcohol withdrawal, largely due to the detailed reports of Victor and Adams (1953) and Isbell *et al*. (1955). In 1955, the WHO acknowledged that 'very serious withdrawal symptoms', such as convulsions or delirium, may follow the discontinuation of a prolonged period of very heavy alcohol intake (Edwards, 1990). In his famous book on the disease concept of alcoholism, Jellinek (1960) referred repeatedly to the WHO reports and placed the adaptation of cell metabolism, tolerance and the withdrawal symptoms at the heart of his alcoholism concept, because they would 'bring about 'craving' and a loss of control or inability to abstain.' In his review of the perception of alcohol withdrawal symptoms in the scientific literature, Edwards (1990) noted that Jellinek's new focus on withdrawal symptoms was 'in very sharp contrast to the earlier stance of the Yale school.' It is possible that it was easier to rediscover the physical complications of alcohol withdrawal, because the new disease concept allowed attribution of these complications to an individual disposition rather than to some general effect that prolonged alcohol intake would have on every consumer.

In Germany, the modern disease concept of alcoholism was promoted by Feuerlein (1967, 1996) and others who emphasized that alcohol-dependent patients should have the same entitlement to medical treatment as other patients. It was not until 1968 that a German federal court formally confirmed full insurance coverage of alcoholism-related medical treatment costs, although alcoholism had already been considered a disease since 1915 (Jellinek, 1960).

ONE OR MANY TYPES OF ALCOHOLISM — GENETIC FINDINGS AND POTENTIAL SUBTYPES

While it had long been observed that the familial risk for alcoholism is increased, it was only because of twin and adoption studies that a genetic contribution to alcoholism was confirmed (Kaji, 1960; Cadoret and Gath, 1978). The observation that family members who share half of their genes are not more likely to develop alcoholism compared with family members who share only a quarter of their genes was incompatible with the simple genetic mechanism of inheritance (Bleuler, 1955; Schuckit *et al*., 1972).

Based on adoption studies, Cloninger *et al*. (1981) suggested the existence of two types of alcoholism, a mostly environmentally triggered, late-onset type 1 and a male-limited type 2 with a high genetic loading, legal problems and moderate alcohol consumption. The attempt to distinguish between two subtypes of alcoholism stimulated considerable research efforts. Many authors, however, questioned the dichotomy and argued that once patients suffering from comorbid antisocial personality disorder were excluded, the distinction between type 1 and type 2 alcoholics no longer offered clinical subtypes with distinct severity (Irwin *et al*., 1990). Instead, subgrouping was suggested to be based on age of onset, the presence of childhood risk factors such as hyperactivity, and severity of alcoholism (Schuckit *et al*., 1995; Johnson *et al*., 1996). Alcoholism types may thus vary on a continuum of severity, rather than represent distinctly different disease entities (Bucholz *et al*., 1996). The genetic disposition to alcoholism may manifest in such unsuspicious forms as a low level of response to alcohol intake in subjects not yet accustomed to chronic alcohol intoxication (Schuckit

and Smith, 1996). A low level of alcohol response has recently been associated with an increased availability of raphe serotonin transporters and a low central serotonin turnover rate (Heinz *et al*., 1998; Schuckit *et al*., 1999). A low serotonin turnover rate is a potential marker of early-onset alcoholism (Fils-Aime *et al*., 1996) and may be caused or aggravated by early social stress experiences (Higley *et al*., 1996*a*,*b*). These findings may help to link the clinical disposition to alcoholism with the growing literature on neurobiological alterations that precede and follow the manifestation of alcohol dependence.

THE CORE OF ALCOHOL DEPENDENCE — TOLERANCE AND WITHDRAWAL OR SENSITIZATION AND REWARD CRAVING?

The last three decades of the twentieth century witnessed a rapidly increasing knowledge of the neurobiological correlates of alcohol dependence. Edwards focused on the development of alcohol tolerance and the manifestation of withdrawal when chronic alcohol intake is terminated (Edwards *et al*., 1977). His groundbreaking work was used by the WHO in the International Classification of Diseases (ICD-9) and operationalized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) as criteria of dependence (Jurd, 1992).

Neurobiological research pointed to alcohol-induced stimulation of inhibitory GABAergic, and the inhibition of excitatory glutamatergic, neurotransmission (Koob, 1992; Tsai *et al*., 1995). To ensure homeostatic regulation, $GABA_A$ receptors may be down-regulated and, indeed, brain imaging studies observed reduced cortical $GABA_A$ receptors among alcoholics (Abi-Dargham *et al*., 1998). When the sedative effects of alcohol are suddenly withdrawn during early abstinence, reduced GABAergic inhibition and increased glutamatergic excitatory neurotransmission may manifest as anxiety, seizures and autonomic dysregulation (Tsai *et al*., 1995). Alcohol consumption may then be reinstated to reduce withdrawal, thus acting as a negative reinforcer (Edwards, 1990). Associative learning may transform neutral emotional or environmental stimuli into alcohol-associated cues that induce a conditioned compensatory response to alcohol, 'conditioned withdrawal', and craving (Ludwig *et al*., 1974; McCusker and Brown, 1990). Acamprosate, a drug used to reduce craving in abstinent alcoholics, blocks glutamatergic *N*-methyl-D-aspartate receptors and may exert its therapeutic effects by decreasing conditioned withdrawal (Verheul *et al*., 1999).

However, cue-induced craving is only moderately associated with the severity of physical reactions such as changes in heart rate and skin conductance to cue presentation (Niaura *et al*., 1988). A secondary, potentially independent pathway has been suggested that may induce alcohol craving due to the mood-enhancing, positive-reinforcing effects of alcohol consumption (Wise, 1988; Koob and Le Moal, 1997). This pathway seems to involve the so-called dopaminergic reward system and its opioidergic stimulation via μ-opiate receptors (Spanagel *et al*., 1992; Di Chiara, 1995). The role of the dopaminergic system may lie in the direction of attention towards reward-indicating stimuli, rather than in the induction of euphoria or positive mood states (Schultz *et al*., 1995; Berridge and Robinson, 1998), which are associated with alcohol consumption and may be mediated by opioidergic neurotransmission (Volpicelli *et al*., 1995). Stimulus-dependent dopamine release may be specifically vulnerable to sensitization, thus mediating a stronger behavioural response upon re-exposure to the drug-associated cue (Robinson and Berridge, 1993). These observations may have important implications for our understanding of the 'addiction memory' and for therapeutic strategies: systematic cue exposure and response prevention might help to extinguish conditioned craving, although therapeutic study results so far are ambiguous (O'Brien *et al*., 1998), and naltrexone medication may prevent cue-induced reinstatement of alcohol craving (Katner, 1999).

THE DISEASE CONCEPT REVISITED

The focus on cue-induced craving and the underlying learning mechanisms (Glautier *et al*., 1994; Carter and Tiffany, 1999) has revived the discussion on whether the disease concept of alcoholism should be replaced by a social learning perspective (Heather, 1992). What was not being denied are the organic consequences of chronic alcohol intake, such as brain atrophy (Mann *et al*., 1995) or neuroadaptive processes such as a reduction of central dopamine D2 receptors (Volkow *et al*., 1996). Rather, it is argued that cigarette smoking similarly causes physical dependence or neuroadaptation without therefore being considered a disease. The disease concept may label patients and promote apathy associated with the 'sick role' (Heather, 1992).

A response to these concerns rests on several arguments. Firstly, it is argued that the sick role *per se* does not stigmatize patients and that the stigma associated with specific diseases such as 'consumption' never promoted similar attempts to deny its disease status, and instead promoted relabelling as tuberculosis (Keller, 1976). Secondly, it is argued that a state may be called a disease even in the absence of abnormalities of anatomic structure. A case in point may be essential hypertension, which is commonly understood as a disease, although the aetiology and pathogenesis are currently unknown. Keller (1976) suggested calling alcoholism a disease, because its behavioural manifestations represent a disablement. This argument resembles the concept of a mental disorder given by the American Psychiatric Association (1987), which argued that a mental disorder is characterized by present distress, disability, or a significantly increased risk of suffering death, pain, disability, or an important loss of freedom. Culver and Gert (1982) added that the state must exist 'in the absence of a distinct (external) sustaining cause', so that distress due to political oppression may be distinguished from a mental malady. Applying this definition to cigarette smoking indicates that smoking should be considered a mental disorder, as it is associated with the increased risk of suffering death, and it would thus be considered a malady or disease by Culver and Gert (1982). This brings up the question of whether fast driving then must be called a disease, as it increases the risk of dying in a traffic accident. It could be answered that the association between fast driving and traffic accidents is rather low and that the habit of driving fast might be terminated without experiencing the distress associated with drug withdrawal symptoms.

As aloof as these discussions sometimes appear, they have important implications for the treatment of alcoholism. In 1956, a Board of the American Medical Association (AMA)

passed a resolution that urged hospitals to admit patients with alcoholism equally with patients treated for other diseases. This act is usually seen as the moment when alcoholism was formally recognized as a disease in the United States; however, alcoholism was already listed as a disease in 1933 in the Standard Classified Nomenclature of Diseases, which was approved by the AMA and the American Psychiatric Association (Keller, 1976). Yet the 1956 resolution highlights the important legal issues that are associated with the disease status of alcoholism, not least being the question of whether treatment costs should be covered by health insurances (Jurd, 1992). Research in the field of costs and benefits of alcoholism therapy supported the demand to treat alcoholism within the medical system (Holder, 1998).

NEW TREATMENT OPTIONS AND FUTURE DIRECTIONS

The last decade of the 20th century witnessed substantial progress in treatment options and strategies. Of special importance is the general practitioner, who sees the vast majority of patients with alcohol problems, while fewer than 10% actually enter specialized treatment programmes (Wienberg, 1992). Brief interventions in primary health care institutions are very often effective in reducing alcohol consumption (Bien *et al*., 1993). For those patients who need more extensive treatment, primary health care services have a gatekeeper function. Motivational enhancement in primary health care (Miller and Rollnick, 1991) can effectively increase the participation in treatment programmes and was associated with reduced subsequent relapse rates (Bien *et al*., 1993). Specialized treatment programmes were evaluated in project MATCH. Project MATCH examined three treatment options, cognitive behaviour therapy, twelve-step facilitation according to the AA programme and motivational enhancement therapy, and found them similarly effective (Project Match Research Group, 1998). As disappointing as this result may be for the discovery of prospective indicators of treatment response, it shows that the major treatment options available to alcoholics worldwide work successfully and that the eclectic combination of behaviour therapy and the attendance of self-help groups may indeed combine two powerful treatment strategies. With naltrexone and acamprosate, two pharmaceuticals are available that successfully reduce the relapse risk during early abstinence (O'Malley *et al*., 1996; Sass *et al*., 1996). However, even with an accompanying medical treatment, most alcoholics relapse. The goal of the future will therefore be to describe subgroups of patients that may respond positively to specific medications. As acamprosate and naltrexone affect different neurotransmitter systems, neurobiological screening of alcoholics may help to discover predictors of treatment response. Preliminary results indicate that sleep disorders, EEG activity and delayed recovery of dopamine receptor sensitivity during early abstinence are associated with the relapse risk and may help to identify patients who require specific treatment strategies (Bauer, 1994; Heinz *et al*., 1996; Brower *et al*., 1998; Winterer *et al*., 1998).

Basic research has profoundly helped to understand alcohol effects at the level of signal transduction. We now know that drugs affect neurotransmitter release, receptor sensitivity, post-synaptic second-messenger mechanisms and, perhaps most importantly, gene expression (Koob, 1992; Nestler, 1994). These observations indicate that human fate is not passively determined by the genetic constitution, but rather that biological and ultimately environmental stimuli regulate gene expression. Increasing knowledge of the molecular mechanisms of dependence may enable us to target these pathological conditions more specifically than we are able today.

Finally, the history of the last 100 years warns us that 'ethics are not an option,' as Edwards stated in a 1999 conference at the Central Institute of Mental Health, Mannheim. That alcoholism had been considered a disease in Germany since 1915 (Jellinek, 1960) did not prevent the dehumanizing treatment of patients with alcohol dependence during the Nazi era. It is an integral part of the professional mission to assist patients in their effort to be treated equally inside and outside of medical therapy. Our increasing knowledge about the disposition towards alcohol dependence and a high relapse risk can help to identify patients with demands for special therapeutic efforts, it should never be used to stigmatize these subjects. To monitor the consequences of our research is part of the professional duty.

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