



The ERAB Board Members: Prof. Kari Poikolainen, Dr Giovanni Addolorato, Prof. Wolfgang Koenig, Mrs Janet Witheridge, Prof. Philippe De Witte, Dr Matty Weijenberg and Dr Chris P. Day.

This book reflects a harmonious relationship between the academic world and the European brewing industry. Despite the fact that they appear to be driven by divergent perspectives, they both agree that ignorance may lead to prejudice. Assumptions made about alcohol, and beer in particular, are often based on media coverage, cultural stereotypes and even myths, without any relevant in depth scientific analysis.

ERAB: The European Foundation for Alcohol Research (ERAB) is proud to provide a step forward to enhance the knowledge of the effects of beer and alcohol on the body and the brain as well as the analysis of the best strategies to reduce, in the short and long term, the possible damage induced by its use.

The beneficial effects of moderate alcohol consumption in terms of cardiovascular disease together with the detrimental effect in terms of cancer, lead to the assumption that consumption must be evaluated personally, taking into account the contextual environment, the global body state and the consensual pleasure arising from its consumption.

"In today's world, we seek to understand, through scientific inquiry, why people drink, why some drink more than others, and why some drink despite negative consequences. Such scientific inquiries require the exploration of multiple spheres of influence ranging from genetic susceptibility to environmental risk within the context of prevailing socio-cultural norms. To this end, ERAB the European Foundation for Alcohol Research is an outstanding example of how the brewing industry and academia are working together to address these issues of mutual concern in contemporary European societies." Professor TK Li, Former Chairman of Scientific Advisory Council of ABMRF, Former Director of NIAAA, NIH.



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Edited by Philippe De Witte

Preface

Mack Mitchell and Oliver F.W. James

- Understanding the effects of alcohol on human health and behaviour is a matter of importance to all members of society.
- ERAB was formed in 2003 to address this issue through research.
- ERAB followed in the footsteps of ABMRF which was founded in 1982 in North America when little was known about the effect of moderate alcohol consumption on health and behaviour.
- The foundation of ERAB represents a milestone in the evolution of collaboration between industry and academia in engaging in independent research that is driven by the important need to achieve better understanding of how products such as beer and other alcoholic beverages, affect the health of society.

Introduction

Philippe De Witte

(Université catholique de Louvain – BE)

- This book reflects the harmonious relationship between the academic world and the European brewing industry.
- Despite the fact that they appear to be driven by divergent perspectives, they both agree that ignorance may lead to prejudice.
- To balance the beneficial effects in terms of cardiovascular disease and the detrimental effects, for example, in terms of cancer alcohol consumption must be evaluated personally taking into account the contextual environment, the global body state and the consensual pleasure arising from its consumption.

Brain, behaviour, genetic findings and pharmacological treatment in alcohol dependence

Giovanni Addolorato

(Alcoholism Treatment Unit, Catholic University Roma – IT)

- This chapter reviews the literature on the role of the neurotransmitter systems in the neurobiology and treatment of alcohol dependence as well as the influence of genetic factors on these neurotransmitter systems.
- To date, only three medications have been approved for treating alcohol dependent individuals, namely disulfiram, naltrexone and acamprostate.
- Their efficacy is modest and the results published in the literature have been, in some cases, inconsistent or even controversial.
- There is a crucial need to identify factors which may predict a better response of patients to certain medications.
- Pharmacotherapies are moving towards the discovery and development of treatment strategies that maximize a medication's alcohol deterrent effect and prolong periods of abstinence in alcohol dependent individuals.
- Genetic components play an important role and there is strong evidence that alcoholism runs in families.
- The rapid advancement of genetic knowledge provides an important opportunity to move towards a significant understanding of the contribution genes have to the development of alcohol dependence.
- ERAB funded studies have helped in the understanding of different genetic pathways, the mechanisms of alcoholism and the effectiveness of pharmacotherapies, usually associated with other conditions, on reducing alcohol consumption in particular groups of patients.

Alcohol and its effects on cardiovascular system

Wolfgang Koenig

(Dept of Internal Medicine II – Cardiology – Ulm University – DE)

- This chapter summarizes the available evidence for cardiovascular effects of alcohol consumption, focusing on the immune system, and anti-inflammatory mechanisms in particular.
- There is substantial experimental, clinical, and epidemiological evidence that moderate consumption of alcohol, through various mechanisms may beneficially affect cardiovascular health.
- The main mechanisms include anti-inflammatory effects, an increase in HDL cholesterol, and anti-thrombotic effects.
- The evidence suggests a causal link between moderate alcohol consumption, and its effects on the immune system and cardiovascular disease morbidity and mortality.
- In recent years ERAB has funded several research proposals related to potential anti-inflammatory effects of ethanol itself or various polyphenols contained in alcoholic beverages and more specifically, the effect of alcohol intake on the metabolism of essential fatty acids in several large populations.
- More recent data from experimental studies further suggest that anti-apoptotic, anti-proliferative, and anti-migratory effects might also play a role, possibly mediated by polyphenols contained in various alcoholic beverages including beer and wine.
- Essential fatty acids like omega-3 fatty acids have also been shown to be increased by moderate amounts of alcohol and several studies are in support of a beneficial effect of increased circulatory levels of these compounds.
- Excessive alcohol consumption is certainly associated with adverse effects on the cardiovascular system as well as on many other organs in the body.
- Further research is needed to address questions concerning the effect of dose dependency, type of beverage and pattern of intake on the mechanisms discussed in order to allow a balanced view of the beneficial effects and the potentially adverse effects of alcohol consumption on the cardiovascular system.

Heavy alcohol intake episodes: determinants and interventions

Kari Poikolainen

(Finnish Foundation for Alcohol Studies – Helsinki – FI)

- This chapter reviews recent research on risk factors for heavy alcohol intake episodes (binge drinking) and the practice and effectiveness of brief interventions to reduce consumption and suggests future research directions.
- Occasional binges increase the risk of acute social and health problems while frequent episodes add to this the increased risk of chronic disease.
- The frequency of binges can sometimes be a better predictor of harm than long-term average intake
- Approaches to reducing harm include brief interventions to reduce alcohol intake and reducing risk factors.
- Risk factors may grow out of both genetic and environmental factors and their interplay.
- Heavy alcohol intake episodes in the offspring are clearly related to parental heavy drinking as well as externalizing and internalizing problems.
- ERAB has funded several studies in this area which have helped us to understand the influence of genetic factors and the effect of several environmental influences.
- Brief interventions have been successful in reducing average alcohol intake among adults under optimal conditions.
- ERAB has funded two studies which have examined the effectiveness of interventions for university students which showed reduced intake per occasion in the groups studied compared to control groups.
- In everyday conditions the effectiveness of brief interventions is smaller or does not exist.
- Future directions for research of this subject include the need to include all the most important risk factors in the analysis together with the amount of alcohol consumed as well as the rate of consumption. Additionally the tailoring of interventions to special risk groups is suggested.

Alcohol and the risk of cancer

Matty Weijnenberg

(Dept. of Epidemiology – Maastricht University – NL)

- This chapter focuses on alcohol consumption and the risk of different cancers.
- Alcohol is a major determinant of life-style health.
- Moderate alcohol consumption is associated with reduced risks of cardiovascular disease but may also increase the risk of several types of cancer, in particular cancers of the head and neck, oesophagus, colorectum and breast.
- Upon ingestion, alcohol is absorbed from the small intestine and taken up into the blood from where it is rapidly distributed over all organs and body fluids.
- Enzymes metabolise (convert) the alcohol first into acetaldehyde, a highly reactive, toxic and carcinogenic metabolite (substance), and then to ALDH, a less active substance that is further degraded to water and carbon dioxide for elimination. Genetic variations lead to different rates of metabolism.
- The liver is the main organ for metabolizing alcohol. Some breakdown of the alcohol is also done by saliva in the mouth and microflora in the colon leading to higher levels of acetaldehyde in these areas.
- The formation of acetaldehyde in alcohol metabolism, and the results of experimental studies in animals and observational studies in humans, have led to the classification of both alcoholic beverages and ethanol in alcoholic beverages as group 1 mixture and agent, respectively, being carcinogenic to humans by the International Agency for Research on Cancer (IARC) in 2007.
- The exact mechanisms by which alcohol invokes the carcinogenic process are still not fully understood and probably differ by target organ. For example the relationship with breast cancer may be associated with higher blood oestrogen levels and the synergistic effect of smoking and alcohol consumption may be due to alcohol acting as a solvent for other carcinogens.
- ERAB funding has helped the understanding of the way that alcohol may be associated with cancer in a number of different areas and in particular has clarified that the increased risk of colorectal cancer associated with alcohol consumption is not beverage specific.
- There are still numerous issues in the research on alcohol and cancer that need to be addressed. These include studies of the effect of different drinking patterns and the role of different beverages. Additionally the analysis needs to address residual confounding and the effect of genetic variation and pooling of data will be essential to provide sufficient sample size.

Alcoholic liver disease

Chris P. Day

(Institute of Cellular Medicine – Newcastle University – UK)

- This chapter sets out the stages of alcoholic liver disease (ALD) together with their clinical features, prognosis and treatment.
- It is likely that humans have been consuming alcohol in excess since the Stone Age and the ancient Greeks made the link between alcohol and liver damage.
- ALD is currently the most common cause of liver disease in the western world and ranges from fatty liver (steatosis) through alcoholic steatohepatitis (ASH) to fibrosis, cirrhosis and hepatocellular carcinoma (HCC).
- End stage liver disease is the result of prolonged heavy alcohol intake in only a small proportion of drinkers.
- Obesity increases the risk of all stages of liver disease in heavy drinkers and genetic factors also contribute to an increased risk.
- Treatments for alcohol dependent patients aim to reduce consumption preferably to zero. Measures include psychological treatments, for example, brief interventions have been shown to significantly increase the chances of heavy drinkers moderating their drinking, and pharmacological treatments, for example, drugs can reduce alcohol craving.
- ERAB funded studies have contributed to an increased understanding of pathogenesis, disease susceptibility and treatment.
- Further research to understand the basics of hepatocyte injury are required to fuel further clinical trials and improve mortality in this disease.