REPORT 2010

ERAB

The European Foundation for Alcohol Research

EDITORIAL

2010 has been an important year for ERAB: The European Foundation for Alcohol Research. Included in the highlights of this year are ERAB's first publication, a new electronic newsletter and the organisation of ERAB's second International Medical Advisory Group Conference (IMAG).

The IMAG Conference, which was held in Frascati in Italy in October, was an opportunity for many of ERAB's grantees to present their research to an international audience. In addition leading experts reviewed key subject areas and helped to put the work funded by ERAB into context. A short résumé of the conference appears at the end of this report. We would like to take this opportunity to thank all the Session Chairs and Speakers at the conference.

ERAB's first publication, New Frontiers in Alcohol and Health, shows how far ERAB has travelled since it was founded by The Brewers of Europe in 2003. The five chapters, written by the Advisory Board members, describe ERAB funded research within an overview of each subject demonstrating the diversity and scientific value of the studies funded.

Through the good offices of The Brewers of Europe, ERAB has been fortunate in maintaining the same level of subscription funding provided in previous years and, in the current economic climate, this is an achievement which is to be commended. This has enabled ERAB to maintain the same level of research support and, with the help of The Brewers of Europe, hold a major conference. At the same time we are seeing an increasing number of high quality applications for funding but can fund only a fraction of those which qualify. Of the thirty nine applications received in 2010 at least half were of very high quality but we were able to fund only those four which were outstanding. This has led the Board of Directors to begin to explore additional sources of funding and collaboration with other Foundations, applying for European Commission Funding and providing the opportunity for sponsors to make donations directly from the website are all being considered.

We look forward to being able to report progress but in the meantime it gives us great pleasure to commend this report to you.

Emeritus Professor
Oliver James
Chairman, ERAB
Board of Directors

Professor
Philippe De Witte
Chairman, ERAB
Advisory Board

NEWS

THANKS

Dr. Kari Poikolainen

Kari joined the ERAB Advisory Board in 2006 and has been an active member for four years. He retired from the Board after the International Medical Advisory Group Conference this October following his retirement from the Finnish Foundation for Alcohol Studies, Helsinki, Finland, where he was the research director. Kari's background in addiction medicine has been invaluable to the Advisory Board where he has been responsible, in particular, for advising on psychosocial research applications. ERAB would like to thank Kari for his expertise and support and wish him a fulfilling and happy retirement.

Mrs. Heidrun Piwernetz

Mrs. Heidrun Piwernetz, the Head of Representation of the Free State of Bavaria to the European Union was a member of the ERAB Board of Directors from November 2007 to April 2010. She resigned from the Board due to her appointment as Director of the Bavarian Representation in Berlin. ERAB would like to formally thank Mrs Piwernetz for her support and helpful advice.

NEWSLETTER

The new ERAB newsletter was launched at the end of 2009 and is sent to almost 500 European scientists who have applied to ERAB for funding, or have helped with the peer reviews. There have been three issues to date which have notified this community of application deadlines and research applications which have been granted. It helps to maintain the visibility of ERAB and strengthen its profile. Copies of the newsletters are also available on the ERAB website http://www.erab.org/asp2/index.asp

SPONSORSHIP OF TRAVEL STIPENDS FOR ALCOHOLISM AND STRESS CONFERENCE

ERAB is providing 5 partial travel stipends for attendees of a meeting in Volterra, Italy in May 2011 - Alcoholism and Stress: A Framework for Future Treatment Strategies, 3 - 6 May, 2011, http://volterraconference.com/home.html

PUBLICATION - NEW FRONTIERS IN ALCOHOL AND HEALTH

To mark its first seven years, ERAB has published a book, "New Frontiers in Alcohol and Health", edited by Professor Philippe De Witte. There are five main chapters written by members of the ERAB Advisory Board. Each presents the research funded by ERAB with its added value in the context of the body of knowledge in that area.

"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.

The book can be obtained on line at a cost of €16.50 for a paperback and €11.00 for a pdf in English http://www.i6doc.com/en/livre/?GCOI=28001100582460 or in French http://www.i6doc.com/fr/livre/?GCOI=28001100582460

A leaflet summarising the contents of the book has also been produced. This is available from the ERAB website www.erab.org

APPLICATION FOR EU FUNDING

Earlier this year the European Commission's DG RELEX (Department for External Relations) sought proposals, in collaboration with a partner in the USA, on, amongst other things, underage drinking. ERAB, in collaboration with ABMRF/The Foundation for Alcohol Research in the USA, submitted a proposal to look in depth at under-age drinking and, how it differs between the two continents. The proposal drew on the expertise in both foundations and with a series of conferences and workshops aimed to deliver recommendations applicable to public health departments in individual countries. Included in the deliverables was a comprehensive website with information for the target age-group and areas for parents and researchers. Sadly, on this occasion, the application was not successful.

INTRODUCTORY INFORMATION

The European Foundation for Alcohol Research was established as an independent Charity in Brussels in 2003 to fund European biomedical and psychosocial research into the effects of beer and other alcohol beverages.

KEY PERFORMANCE INDICATORS 2003 - 2010

Total subscriptions to end 2010	€ 3,732,100
Total grant spend to end 2010	€ 3,328,751
Total Applications	226
Total full grants funded	45
Number of two year grants	37
Number of biomedical grants	30
Number of psychosocial grants	15
Number of publications citing ERAB	81
Total Travel Award Applications	58
Number of Travel Awards funded	39
Total Exchange Award Applications	10
Number of Exchange Awards funded	8

To date ERAB grants have been undertaken in 11 different EU countries. Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Portugal, Sweden, Switzerland and UK.

THE ERAB WEBSITE

The ERAB website includes; biographies of the members of both Boards; information about how to apply for a grant, including the deadlines; details of grants already funded; the publications resulting from these grants and proforma report forms for grantees to download. It also provides links to the newsletters and other ERAB publications.

The website receives a growing number of visits each year - almost 168,300 in 2010 an increase of 34% on 2009. This activity peaks in the Spring when grant applications are due and shows that it is being consulted by the research community.
www.erab.org

CONTRIBUTORS

Without the continued support of the European Brewing Sector, ERAB would not be able to continue to fund independent research into the biomedical and socio-behavioural aspects of alcohol consumption.

This year, for the first time, subscriptions to ERAB have been received from all 27 member associations of The Brewers of Europe as well as the four major brewers in Europe. ERAB would particularly like to thank its new supporters while gratefully acknowledging the continued support of longstanding contributors:

- **APCV - Associação Portuguesa dos Produtores de Cerveja, Portugal;**
- **Association of Hungarian Brewers, Hungary;**
- **Associazione degli Industriali della Birra e del Malto, Italy;**
- **Beer and Malt Producers´ Association of Turkey, Turkey;**
- **Belgian Brewers, Belgium;**
- **Brasseurs de France, France;**
- **Brewers of Romania, Romania;**
- **Bryggeriforeningen, Denmark;**
- **Cerveceros de España, Spain;**
- **Cyprus Brewers Association, Cyprus;**
- **Czech Beer and Malt Association, Czech Republic;**
- **Deutscher Brauer-Bund e.V., Germany;**
- **Grants Committee of the British Beer & Pub Association and the Institute of Brewing & Distilling, UK;**
- **Fédération des Brasseurs Luxembourgeois, Luxembourg;**
- **Greek Brewers' Association, Greece;**
- **Lithuanian Breweries Association, Lithuania;**
- **The Malta Chamber of Commerce, Enterprise and Industry, Malta;**
- **Nederlandse Brouwers, The Netherlands;**
- **Norwegian Brewers, Norway;**
- **Irish Brewers' Association, Ireland;**
- **Panimoliitto, Finland;**
- **Slovak Beer and Malt Association, Slovakia;**
- **Sveriges Bryggerier AB, Sweden;**
- **Swiss Breweries´ Federation, Switzerland;**
- **The Union of Brewing Industry Employers in Poland, Poland;**
- **Union of Brewers in Bulgaria, Bulgaria;**
- **Verband der Brauereien Österreichs, Austria.**

- **The Brewers of Europe;**

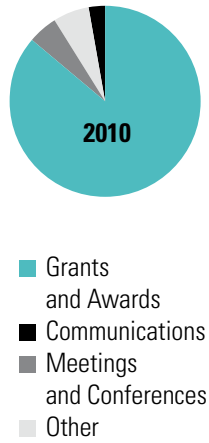
- **Carlsberg;**
- **Heineken;**
- **Anheuser Busch InBev;**
- **SABMiller.**

FINANCE

An average of five grants up to €100,000 are funded each year, together with four or five travel awards, and one or two exchange awards. The research grant expenditure accounts for the majority of the annual budget.

	2004	2005	2006	2007	2008	2009	2010*
	€	€	€	€	€	€	€
Revenue and Support							
Industry contributions	434,500	445,000	425,000	535,000	535,000	474,000	469,000
Investment income	2,365	7,972	1,926	6,098	2,450	110	300
Expenditure							
Grants and Awards							
Grants	390,390	496,600	421,846	426,398	727,315	422,482	391,900
Awards	-	2,500	11,656	12,219	9,504	8,590	7,351
Sub Total	390,390	499,100	433,502	438,617	736,819	431,072	399,251
Other Expenditures							
Communications	9,195	9,334	5,310	17,017	5,490	9,638	12,875
Meetings and Conferences	59,023	33,838	19,222	32,371	13,696	17,078	22,538
Other	5,743	7,077	5,370	5,562	5,631	20,208	29,598
Total Expenditure	464,351	549,349	463,404	493,567	761,636	477,996	464,262
Assets carried over	329,354	231,742	195,264	242,795	0	0	0
Reserve					18,608	14,722	19,302
Endowment	25,000	25,000	25,000	25,000	25,000	25,000	25,000

* Provisional



ERAB GRANTS

ERAB invites applications for funding European biomedical and psychosocial research into the effects of beer and other alcohol beverages, by advertising in relevant medical journals, at the beginning of each year. The applications are sent for peer review to experts in the relevant subject from all over the world. The recommendations as to which grants are funded are based on these reviews which give great emphasis to the scientific merit of the application. Grants are now funded up to the maximum of €50,000 for one year or €100,000 over two years.

Of the 41 major grants funded so far, seven were completed at the end of 2006, four at the end of 2007, three at the end of 2008, seven at the end of 2009 and nine by the end of 2010. Seven will be completed in 2011 and four in 2012.

AWARDS FOR YOUNG RESEARCHERS

As well as providing major research grants ERAB is keen to encourage young researchers to work in the field of alcohol research and offers a number of much smaller travel and exchange awards for researchers under the age of 35. The travel awards enable scientists to travel to conferences to present their data. The exchange awards allow periods of study / collaboration in centres of excellence anywhere in the world.

In addition to the above awards for young researchers, small awards may be made available to help publish PhD theses.

2010 GRANTS

At its eleventh meeting on 17th October 2010, the ERAB Board of Directors agreed that the following four research projects should be funded during 2011 / 2012.

Dr. Marianne VAN DEN BREE	University of Cardiff, Department of Psychological Medicine & Neurology, **UK**
Biomedical Two year	Peer group influences on the relationship between depressive symptoms and alcohol misuse in adolescence.
Dr. Salvatore CAMPANELLA	Free University Brussels, Brugmann Hospital, **Belgium**
Biomedical Two year	Binge drinking: Cognitive and brain impairment and their association with immune response.
Dr. Anna GOUDRIAAN	Academic Medical Center, Department of Psychiatry, Amsterdam, **The Netherlands**
Biomedical Two year	Changing the vulnerable brain: a neuromodulation study in alcohol dependence.
Dr. Alessandro ORRU	Institute for Pharmacological Research Mario Negri, Milan, **Italy**
Psychosocial Two year	Role of BDNF signalling in alcohol abuse: new insights from a yoked paradigm.

BOARDS

ERAB has two boards - a Board of Directors, and an Advisory Board.
ERAB is grateful to the members of both Boards who generously give their time and expertise without reward.

BOARD OF DIRECTORS

ERAB's independence is guaranteed by a Board of Directors made up of a majority of public members. Their role is to administer the funds.

CHANGES TO THE BOARD OF DIRECTORS IN 2010

This year, ERAB was pleased to welcome **Mr. Dipl.-Ing. Markus Ferber, MdEP, Member of the European Parliament,** to replace **Mrs. Heidrun Piwernetz,** the Head of the Representation of the Free State of Bavaria to the European Union.

PUBLIC MEMBERS

Emeritus Professor Oliver F. W. James
former Pro Vice Chancellor, Faculty of Medical Sciences, University of Newcastle upon Tyne, UK. **(Founder Member, Chairman).**

Professor Daniel Bessa
COTEC, Portugal.

Mr. Raymond Georis
Belgium **(Founder Member and Past Chairman)**.

Mr. Dipl.-Ing. Markus Ferber, MdEP
Member of the European Parliament, Bavaria.

Mr. Jean Martin
Former President of the European Confederation of the Food & Drink Industry, Belgium.

Professor Mack Mitchell
ABMRF / The Foundation for Alcohol Research, USA.

Dr. Erik Skovenborg
Medical Doctor, Denmark.

Vanessa Witkowski
Belgium.

Professor Philippe De Witte
Université Catholique de Louvain-la-Neuve, Belgium.
Chairman of the ERAB Advisory Board.

Janet Witheridge
ERAB: The European Foundation for Alcohol Research.
Secretary-General.

REPRESENTATIVES OF BREWERS AND TRADE ASSOCIATION OFFICIALS

Mr. Alberto da Ponte
The Brewers of Europe, Portugal.

Mr. Rutger Goethart
Heineken, The Netherlands.

Mr. Simon Jackson
Institute of Brewing and Distilling, UK.

Mr. Jacobo Olalla Marañón
Cerveceros de España, Spain.

Mr. Knud Hedeager Nielsen
Carlsberg, Denmark.

HONORARY MEMBERS (ACCORDING TO ARTICLE 6 OF THE BY-LAWS)

Dr. David Long
Consultant, Former Director Brewing, British Beer & Pub Association, UK.

Count Rodolphe de Looz Corswarem,
Consultant, Former Secretary-General, The Brewers of Europe, Belgium.

Mr. Piero Perron
Heineken, Italy. **(Founder Member)**

Emeritus Professor Richard Smallwood
Former Commonwealth Chief Medical Officer (1999-2003), Australia.

ADVISORY BOARD

The members of the Advisory Board have a proven international independent scientific reputation. Their role is to examine the applications, suggest peer reviewers and recommend to the Board of Directors which applications should be funded.

CHANGES TO THE ADVISORY BOARD IN 2010

This year, ERAB was pleased to welcome **Professor Pekka Sulkunen** from the Department of Sociology at the University of Helsinki in Finland who replaced **Dr. Kari Poikolainen** who retired after the IMAG conference as mentioned above.

Professor Philippe De Witte
Department of Biology, Université Catholique de Louvain-la-Neuve, Belgium. Chairman.

Professor Giovanni Addolorato
Department of Internal Medicine, Università Cattolica del Sacro Cuore, Rome, Italy.

Professor Christopher P. Day
Faculty of Medical Sciences, University of Newcastle upon Tyne, UK.

Professor Wolfgang Koenig
Department of Medicine, University of Ulm, Germany.

Professor Pekka Sulkunen
Department of Sociology, University of Helsinki, Helsinki, Finland.

Associate Professor Matty P. Weijenberg
Department of Epidemiology, Maastricht University, The Netherlands.

PUBLICATIONS RELATING TO ERAB FUNDED RESEARCH

To date ERAB grantees have published the results of the research funded by ERAB in 81 papers in peer reviewed journals. For a full list of publications visit http://www.erab.org/asp2/publications/index.asp

INTERNATIONAL MEDICAL ADVISORY GROUP CONFERENCES

International Medical Advisory Group (IMAG) conferences have been held almost every year since 1972 and offer an opportunity for the Medical Advisors to the brewing sector worldwide to discuss topical issues and recent research advances in the field of alcohol and health.

CONFERENCE REPORT

INTERNATIONAL MEDICAL ADVISORY GROUP (IMAG) CONFERENCE
Frascati, Italy 17th-19th October 2010
Dr. David Long,
Honorary Member of the ERAB Board of Directors.

This 36th IMAG Conference, held in Frascati, Italy (17-19 October 2010) was organised by ERAB. The majority of presentations were given by ERAB grantees, indicated in this report by an asterisk (*). There were more than 100 participants from 17 countries, representing university departments, medical research institutes, brewing companies and brewing trade associations.

SUMMARY

Some key points to emerge from this Conference can be summarised as follows.

- The Conference demonstrated that there are a number of promising treatment strategies in development which focus on those groups that are at risk.
- For example, appropriately timed brief personalised interventions can be effective in addressing the problem of binge drinking amongst individuals who have been identified as being at high risk, e.g. amongst groups of university students.
- By contrast, there is now a body of opinion that "social norms marketing campaigns" to correct the misperception about peer drinking levels are largely ineffective.
- ERAB –funded studies are contributing to an increased understanding of Alcoholic Liver Disease (ALD), susceptibility and treatment. It is apparent that within 15 years, it will be technically feasible to scan the human genome and determine those individuals who are susceptible to alcoholic liver disease ALD.
- Acetaldehyde (from the breakdown of alcohol in the body) has been classified very recently by the World Health Organisation as a causal agent for cancers of the head, neck and throat.
- Consumption of alcohol increases the risk of breast cancer in women. Very large studies that control for other factors show that one drink per day increases the relative risk by a very small amount. Individuals need to consider health risks in the context of their own lifestyle, family history, etc., and in consultation with medical professionals.
- The Conference confirmed that the protective mechanisms of alcohol in relation to cardio-vascular disease are now well understood and the benefits of moderate drinking are widely accepted by the mainstream medical community.

SOCIAL CONTEXT OF DRINKING

Professor Enrico Tempesta, Osservatorio Permanente sui Giovani e l'Alcool, the Chair of the session, stressed the need for research efforts on the effects of alcohol to include relevant anthropological and sociological factors. He said that any alcohol and health policy must take into account the complexities, and place the consumer rather than product at the centre of the policy. Since it has been widely confirmed that alcohol has some positive effects on health it is essential to educate consumers to help them develop a responsible relationship with alcohol in order that they can benefit from the positive effects and avoid the harms.

Dr Karen Trocki, Alcohol Research Group, Emeryville, CA, USA, argued that contexts are important in the study of alcohol consumption. Situations and environments in which people drink are associated with norms, beliefs, attitudes and expectancies. These influence the amount and speed of consumption as well as other behaviours. It has been demonstrated that approximately half the predictive factors in drinking would be ignored if one focused only on the individual without taking drinking contexts into consideration.

BINGE DRINKING

Professor Philippe De Witte, University of Louvain La Neuve, Belgium, the Chair of the session, discussed the importance of studying drinking patterns. He detailed factors that influenced the development of drinking in adolescents; family, peer relationships, gene-environment interactions, brain maturation and sensitivity to alcohol. He said that prevention should focus on family and school in strengthening parenting skills and influencing positive peer relationships. Professor De Witte also discussed the available treatment strategies.

Dr. Patricia Conrod, King's College London, UK (*) and University of Montreal, Canada, described personality-targeted interventions in schools. She demonstrated that when delivered to individuals with high-risk personality profiles, there was a significant delay in the onset of drinking and binge drinking in adolescence and a reduction in the likelihood of taking up illicit drug use over a two-year period.

In a study funded by ERAB she is looking at the effect on the whole class when only a proportion of those in the class receive the intervention. This has the advantage that it does not disrupt class time. Initial results indicate that the positive effect on the high-risk group is transferred to the low-risk late onset drinkers. Thus, there is a "universal" impact from a targeted intervention. This is a novel and potentially important observation for the design of future strategies.

By contrast, there is a growing consensus that "social norms marketing campaigns" to correct the misperception about peer drinking levels have now been shown to be largely ineffective. **Dr. David Foxcroft, Oxford Brookes University, Oxford, UK (*)**, had conducted an exhaustive randomised controlled trial to replicate the best of the previous studies and concluded that for social norms marketing campaigns, the results are on the whole not significant and therefore cannot be recommended.

Professor Roberta J. Ward, Louvain La Neuve, Belgium and Università degli Studi di Firenze, Florence, Italy(*), presented evidence that binge drinking is associated with brain damage resulting from an inflammatory response. It is known that the compound "NFκB" is a key component in this inflammatory pathway. It was therefore postulated that inhibition of NFκB activation during a 'binge drinking' regime would reduce neurotoxicity. The amino acid, taurine, has been shown to inhibit NFκB activation. Evidence was presented which showed that the activation of the innate immune system induced by binge drinking is reduced by the co-administration of the taurine pro-drug ethane-ß-sultam during the ethanol regime.

HEAVY ALCOHOL INTAKE EPISODES

Dr. Kari Poikolainen, Finnish Foundation for Alcohol Studies, Finland, the Chair of the session, analysed the various definitions of heavy alcohol intake episodes which include "heavy drinking", "heavy episodic drinking", "intoxication", "drunkenness" and "binge drinking". The criteria may be based on amount consumed, subjective effects, or blood alcohol levels and there is no general agreement on definitions. Recently, some have started using it to mean a certain number of drinks (typically five or more) consumed during one drinking occasion or sitting. The duration of drinking is critical for the acute effects of alcohol in the brain, and thus behaviour, given a certain level of intake.

Resultant intoxication has been found to relate directly to belligerence, legal, family and social problems, traffic accidents, drunken fights, injuries, and mortality. Even after controlling for the overall level of alcohol intake, consuming 5 drinks or more daily has been found to relate to social problems, driving under the influence, interpersonal conflicts, family disruption and failure to fulfill social roles. Increased risk of stroke, fatal coronary heart disease and total mortality has been found for men drinking 6 or more drinks daily.

Dr. Marianne van den Bree, Cardiff University, Cardiff, UK (*), presented evidence that environmental influences tend to be greater for initiation of consumption, while genetic influences exert considerably stronger influences on the progression to heavier use. She looked at some of the strongest risk factors for adolescent alcohol misuse

including the effects of peer influences and "externalising behaviours" (e.g. conduct problems and aggression) as well as "internalising symptomatology" (e.g. depression and anxiety). Her findings confirm that the developmental pathways to the problem use of alcohol are complex. It was argued that a more detailed understanding of the interaction between factors would inform prevention approaches.

Dr. Solja Niemelä, University of Turku, Finland, advocated studying risk factors over a time period to help identify subgroups of young people at greater risk of substance-use-related problems, and to facilitate targeted prevention efforts. In this study, the population included 10% of all Finnish-speaking boys born in Finland in 1981. Boys with "externalising" problems had elevated rates of substance use in early adulthood. Teacher reports on boys' problem behaviour had the best predictive power for later substance use. Targeted early interventions in school health care systems were recommended.

Professor Javier Ballesteros, University of the Basque Country, Spain, reported that several systematic reviews and meta-analyses had shown that brief behavioural interventions conducted in primary care to reduce the amount of alcohol consumption are effective for at-risk drinkers. His study confirmed that brief interventions, as compared to extended brief interventions, conducted in primary care are effective in reducing alcohol consumption in hazardous drinkers.

PHARMACOLOGICAL TREATMENT OF ALCOHOL DEPENDENCE: FROM BENCH TO BEDSIDE

The session was chaired by **Professor Giovanni Addolorato, M.D. (Catholic University of Rome, Italy).** Professor Addolorato gave an introduction to this area of research and highlighted the fact that there were a number of pharmacological treatments for alcohol dependence currently under active investigation.

Professor Giancarlo Colombo, CNR Neuroscience Institute, Cagliari, Italy (*), argued that there is an ongoing need to develop effective animal models for alcoholism to investigate the neurobiological bases of the disease, as well as to test drugs to treat alcoholism. Binge-like drinking behaviour of intoxicating amounts of alcohol can be successfully induced in Sardinian alcohol-preferring rats which will provide powerful research tools for future investigations.

Professor Otto M. Lesch, Medical University of Vienna, Austria, highlighted some of the key issues to be taken into account when assessing treatments for alcohol dependence. Alcoholism is a heterogeneous condition. However, most countries tend to offer homogeneous programmes of treatment, which are neither evidence-based nor tailored to the individual.

Many different compounds with significantly different actions on the brain have shown positive results (e.g. Acamprosate, Naltrexone, Sodium Oxibate, Baclofen, Topiramate, Sertaline, Disulfiram). All these substances have both positive and negative effects. It is essential to consider specific treatment goals in accessing the efficacy of different compounds. One must consider which alcoholic patient will benefit most from what treatment.

Dr. Lorenzo Leggio, Brown University, Providence, RI, USA and Catholic University of Rome, Rome, Italy (*), reported that advances in understanding alcohol dependence have identified a number of chemical pathways in the brain. Drugs that target these pathways may have the potential to provide effective treatment. For example, the potential role of the drug "Baclofen" is receiving a great deal of attention.

Baclofen has been shown to reduce alcohol consumption and promote abstinence in alcohol-dependent patients. The drug has been associated with reductions in alcohol craving, anxiety, and alcohol withdrawal symptoms. Of special note, to date, Baclofen represents the only medication tested in alcoholics with severe liver diseases (e.g. cirrhosis, hepatitis).

However, some questions remain, including targeting the subgroup which best responds to Baclofen, the potential for higher doses of the drug to be more effective without reducing the safety profile, as well as understanding the mechanisms of how Baclofen works.

Professor Rainer Spanagel, Central Institute of Mental Health (CIMH), University of Heidelberg, Mannheim, Germany, reported that several chemical pathways in the brain have been identified with mediating craving and relapse to alcohol. Interference with these pathways is the focus of a number of drug treatments. For example, "Naltrexone" and "Acamprosate", which act on specific pathways involving opioids and glutatmate, have been shown to be clinically effective. Although the system commonly associated with the reward system of the brain (dopamine) has been a focus of alcohol research for many years, clinical trials with drugs interfering with several components of this system have displayed rather disappointing results. However, this situation could change in light of the discovery of the possible involvement of a specific protein (the D3 dopamine receptor). This is likely to be the subject of further research effort. This German research programme has identified a number of new targets and new compounds, which are currently undergoing clinical testing with a view to developing targeted drug treatments.

ALCOHOLIC LIVER DISEASE (ALD): SUSCEPTIBILITY AND NEW TREATMENT TARGETS

The session was chaired by **Professor Chris Day, University of Newcastle upon Tyne, UK,** Professor Day provided an elegant resume of the complexities of ALD and highlighted the fact that funding by ERAB was contributing significantly to our understanding of this important disease.

Dr. Luca Miele, Institute of Internal Medicine Catholic University of Rome, Rome, Italy (*), posed the question why the majority of heavy drinkers do not go on to develop ALD. Through a complex decision tree, a number of potential candidate genes/genetic variants have been identified as worthy of further study. However, all require confirmation. Dr Miele suggested that this would be best achieved through multicentre/multi-national collaborations.

Genetic susceptibility to ALD is strictly linked to the understanding of mechanistic aspects of alcohol-induced liver injury and may help to design new treatment and prevention strategies to patients at higher risk to progression.

Dr. Steven Dooley, Heidelberg, Germany (*), reported that a particular cell-signalling protein (or cytokine, designated "TGF-β") is higher in blood serum of patients with ALD. The focus of his study was on the involvement of TGF-β in the progress of ALD using a mouse model. Some of the enormous complexities of cell signalling and the challenges in conducting this sort of work were highlighted. The results of this study indicate that ethanol consumption of patients with pre-damaged livers displaying elevated TGF-β levels, will result in enhanced cell death which may accelerate the end-stage of cirrhosis and the development of liver cancer.

Dr. Stuart Kendrick, Newcastle University, Newcastle upon Tyne, UK (*), reported that patients with acute alcoholic hepatitis (AAH) show elevated levels of cytokine in response to lipopolysaccharide stimulation. A novel mechanism was postulated by which ethanol increases histone acetylation, increasing cytokine synthesis.

The data produced in this study suggest that synthesis of acetyl-coA from acetate is critical to the increased acetylation of pro-inflammatory gene histones and consequent enhancement of the inflammatory response in ethanol-exposed macrophages. This mechanism has potential as a therapeutic target in AAH.

Professor Emanuele Albano, University "Amedeo Avogadro" of East Piedmont, Novara, Italy (*), said that it is increasingly recognized that inflammation has an important role in the development of ALD. However, the mechanisms by which alcohol is involved in inflammatory processes are still not completely understood.

A number of experiments with mice have now demonstrated that immune reactions, triggered by oxidative stress, might contribute to the promotion of chronic liver inflammation during the development of ALD. If confirmed by further studies, this could be the basis of a useful non-invasive blood serum test for the identification of patients at risk of ALD progression, potentially with the most to gain from targeted antioxidant therapy.

ALCOHOL AND CANCER

Associate Professor Matty Weijenberg, Maastricht University, The Netherlands, introduced this session which featured a number of important developments.

Dr. C.J. Peter Eriksson, University of Helsinki, Finland, highlighted the fact that acetaldehyde had been classified recently by the World Health Organisation as a "Group 1" carcinogen (i.e. with sufficient evidence to cause cancer in humans) in the oesophagus and head and neck.

This review provided an authoritative update on the genetic-epidemiological evidence for the carcinogenic role of acetaldehyde in these and possible other new sites. The target gene polymorphisms, for this study, were those that affect the rate of acetaldehyde production (i.e. alcohol oxidation) and elimination (i.e. acetaldehyde oxidation).

The strongest evidence for the carcinogenic role of acetaldehyde is derived from the association between the ALDH2*2 allele (which causes an increase in acetaldehyde) and cancer frequency in Asian populations.

There is limited evidence for tumour sites in the colorectum, pancreas and female breast associated with the ADH1B*2 allele (coding highly active alcohol dehydrogenase) in Caucasian populations.

There are convincing data showing that the ADH1B*1 allele (coding more active alcohol dehydrogenase) is associated with oesophageal and head and neck cancers, which has been explained by prolonged duration of the presence of alcohol and related acetaldehyde production.

Dr Eriksson concluded that it is possible the currently established frequency and sites for the carcinogenic effects of acetaldehyde are underestimated especially with regard to gastric, pancreatic and lung cancer.

Dr. Manuela Bergmann, EPIC group, German Institute of Human Nutrition, Potsdam-Rehbrücke, Germany, drew a comparison between alcohol consumption being causally linked to increased risk of cancers of head and neck, colon, rectum, anus, liver, and female breast and moderate alcohol consumption being related to lower risk of cardiovascular diseases (CVD).

The European Prospective Investigation into Cancer and Nutrition (EPIC) provides an opportunity to make a comparison between these effects. The study involved about 500,000 participants. During 10 years of follow-up, information was collected on incidence of cancers and on causes of death. It was concluded that:

- lifetime "always light" or "never heavy" alcohol consumption may exhibit the lowest risk of both cancer and CVD;
- Potential health benefits of alcohol may depend on past alcohol consumption levels; and
- heavy alcohol use at any point in life seems to be an additional risk factor for cancer, and probably for CVD as well.

The authors recommended that public health initiatives to lower alcohol consumption should start in early adulthood and focus on the prevention of heavy alcohol consumption during any period of life.

Dr. Mirjam Heinen, Maastricht University, Maastricht, The Netherlands (*), drew attention to the fact that consuming alcoholic beverages may reduce the risk of lymphatic malignancies (LM), though the evidence for this assertion is sparse.
Her study aims to assess whether:

- alcohol consumption decreases the risk of LM; and
- decreased risk is due to alcohol or other components of alcoholic beverage types (i.e. beer, wine, and spirit).

These questions were being addressed within the framework of the large-scale prospective Netherlands Cohorts Study on Diet and Cancer. It was anticipated that this on-going study would provide new insights into the role of alcohol in relation to the risk of LM at the population level.

CARDIOLOGY AND ALCOHOL

The session was chaired by **Professor Manuel Carrageta, Portuguese Foundation of Cardiology, Portugal.**

Professor Wolfgang Koenig, University of Ulm, Germany, confirmed that moderate consumption of alcohol has been found to be consistently associated with reduced risk for fatal or non-fatal heart attack, sudden cardiac death, and consequently all-cause-mortality. Several recently published large meta-analyses from well controlled representative prospective epidemiological studies strongly confirm such earlier findings. Favourable effects on the lipid profile, such as increased levels of high-density-lipoprotein (HDL) cholesterol, and blood indicators, such as increased tissue-type plasminogen activator (t-PA) and decreased fibrinogen, explain only half of the beneficial effects of moderate alcohol consumption on Coronary Heart Disease (CHD) risk.

Other factors must be involved. The effects of alcohol consumption on the immune system have been known for some time. Since thickening of artery walls in atherosclerosis is indicative of an inflammatory disease, an anti-inflammatory and anti-oxidative action of moderate alcohol consumption has also been suggested. Other mechanisms include inhibition of smooth muscle cell proliferation and inhibition of white blood cell migration, both important steps in the build-up of an atherosclerotic plaque.

This presentation summarized the current evidence base for cardiovascular effects of alcohol consumption, focusing on the immune system and anti-inflammatory mechanisms in particular. Such data suggest a causal link between moderate alcohol consumption, and its positive effects on the immune system and protection against cardiovascular disease morbidity and mortality.

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