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In this issue

Editorial 1

Dr Dominique Florin:
Introductory message

Dr Guy Ratcliffe:
Valedictory message

Winning entries from
National Alcohol
Awareness Day
competition 2010 2

Steroid resistance in
severe alcoholic
hepatitis 3

General Election 2010 4

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FROM THE EDITOR



Dr Dominique Florin

Introductory message

I am delighted to take up the post of medical director of the MCA. Many thanks to my predecessor Guy Ratcliffe for his support in this transition period. I intend to continue the regular publication of this newsletter, and would welcome any contribution or feedback from our readers.

My own background is in primary care and public health, and I worked for many years on health policy at the King's Fund. I still work in an inner city general practice, and have plenty of exposure to the problems of alcohol excess.

This feels like an exciting time in the area of alcohol policy and practice. There is a growing recognition of the effective interventions which could significantly reduce the negative

impact of alcohol. The actions of those working at all levels in the alcohol field will be central, and I am looking forward to contributing to the MCA's role in confronting this challenge. In June we ran a very successful symposium on 'Alcohol and the Brain', which was attended by over 100 medical and non-medical alcohol professionals. The MCA has just published a new edition of the handbook *Alcohol and Health* by Marsha Morgan and Bruce Ritson, which is being distributed to medical students through their medical schools.¹ The MCA's journal *Alcohol and Alcoholism* continues to go from strength to strength, contributing to alcohol research. In my new role I would like to build on Guy's links with medical students; on the work by colleagues on the undergraduate curriculum; on the MCA's links with organisations for health professionals misusing alcohol, such as the Practitioner Health Programme; and on our relationships with other alcohol organisations, particularly through the Alcohol Health Alliance. I hope our members will let me know any other thoughts!

References

- 1 Morgan M, Ritson EB. *Alcohol and health: A guide for health-care professionals* (5th edn). London: MCA, 2010.

Valedictory message

This is my last editorial for *Alcoholis*, the MCA's newsletter which was reintroduced in 2006. It has been a challenge and a pleasure to produce articles and comments that are relevant and educational as well as interesting and, hopefully, thought-provoking. I wish to express my thanks to all those who have contributed articles, comments and helpful advice to its production over the last 5 years. I must identify Caroline Marris and Katie Fay as the key players in the MCA office for coping with my foibles and eccentricities, as well as ensuring that production deadlines are achieved most of the time. Of equal importance has been Suzanne Fuzzey of the Publications Department of the RCP. To her and to all members of her team I wish to express my thanks for all their efforts with design, proof reading and all the other issues that need to be addressed in producing a very worthwhile publication. To readers who have not contributed I would urge you to consider an article, an opinion or an anecdote relevant to the MCA.

Finally I welcome my successor, Dr Dominique Florin, as the medical director of the MCA, who inherits editorial control of your newsletter from the next issue.

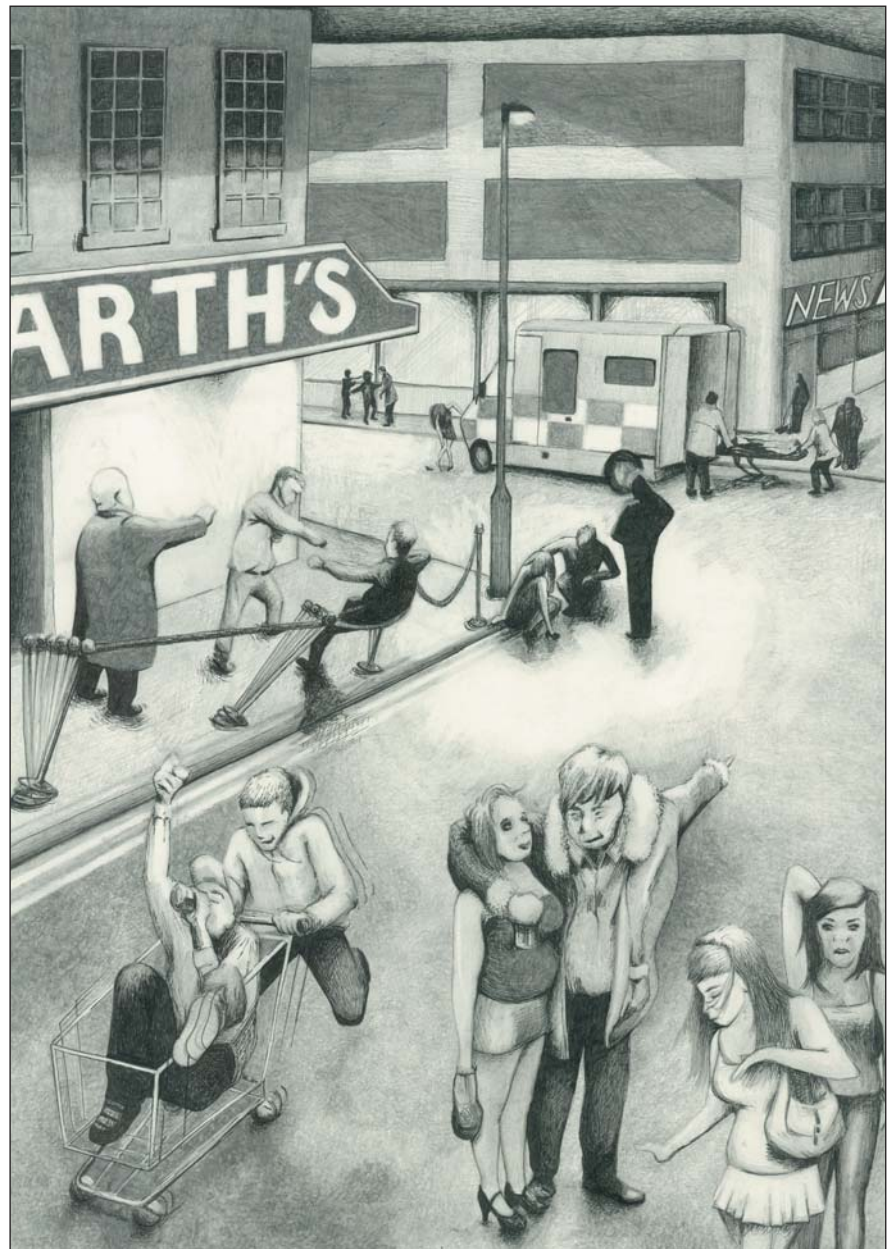
Dr Guy Ratcliffe

Winning entries for the National Alcohol Awareness Day competition

The format for this biennial prize for medical students was changed for the third running of this competition. As was reported in the last issue of *Alcoholis* for 2009, the competition invited medical students to produce a poster depicting a 21st century version of Hogarth's *Gin Lane* and *Beer Street* etchings published in 1751.

The etchings were produced to coincide with the Gin Act of that year, within which legislation was introduced to control more tightly the sale of gin, thereby reducing the impact of the consumption of alcohol, particularly imported gin in London. English-produced ale was promoted as a healthier alternative, hence *Beer Street*. Below each etching were printed lines of verse by Townsley, damning the evils of gin or recommending beer respectively.

The competition, which was organised in conjunction with the BMA Medical Students Welfare Committee, attracted several entries. Students were allowed to use a variety of media as they saw fit. Thanks are expressed to the Medical Illustration Department of the Royal Free Hospital, whose staff made a great contribution to the judging of design, format and appropriate use of a variety of media. Some entries were joint, others concentrated on one aspect of *Gin Lane*, not least the image of the woman in the foreground, clearly inebriated to the extent of allowing her child to fall to its inevitable death down some stairs. These entries concentrated therefore



▲ WINNER: *Arth's*, a pencil etching by Kelly Jones, Warwick University

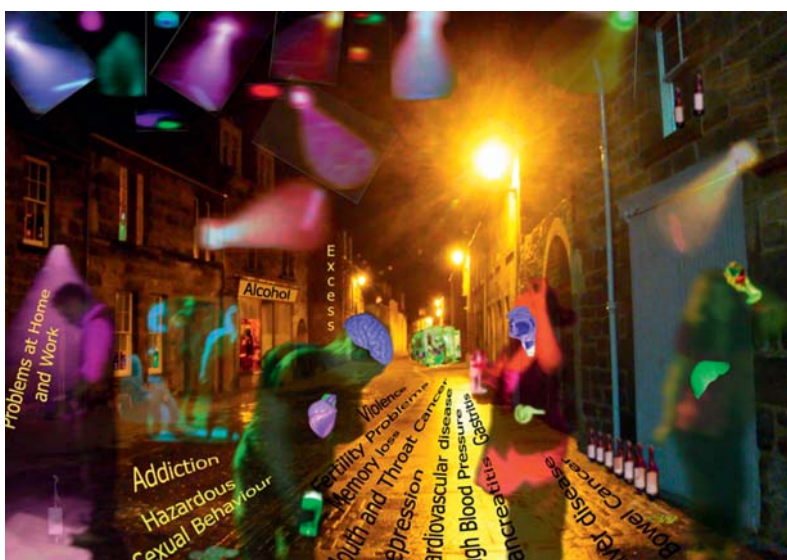


▲ SECOND PLACE: *Binge Alley*, by Matt Stubbs and Tia Radosavljevic, Royal Free and UCL Medical School

► **THIRD PLACE:** A street scene including target organs, by Alex Kennett, University of St Andrews

on foetal alcohol syndrome. Although very powerful messages resulted, the judges unanimously felt that these entries did not accurately reflect the overall public health message suggested by the title of the competition. Nevertheless, the judges were very praiseworthy of all entries.

The winning posters are reproduced here. Congratulations to the winners, who will be spending 3- to 4-week placements learning about the management of addiction later this year.



Steroid resistance in severe alcoholic hepatitis

Dr Peter Collins, Consultant Hepatologist

Alcohol-related mortality is steadily increasing, and the rate of alcohol-related liver disease has doubled over the last 10 years. It is estimated that 84% of liver disease-related deaths are attributable to alcohol. Heavy alcohol intake can lead to a variety of liver disease, with acute or chronic damage. Severe alcoholic hepatitis is an acute liver injury that is associated with a high mortality rate. The condition is characterised by a severe inflammation within either a normal or chronically damaged liver. Despite improvements in our understanding of the underlying disease processes, and the care of patients with liver injury, a significant number of patients with severe alcoholic hepatitis will die within 3 months.

Many hepatologists believe that steroid treatment can help to reduce inflammation and improve survival in alcoholic hepatitis, although this is not universally accepted. Studies show that treatment with oral prednisolone can increase survival from 65% to 85%. Despite this apparent success, there is a group of patients who do not respond to steroid treatment and who have a high chance of death (up to 70%). There is currently no good way to identify patients who are resistant to the effects of steroids early in their

hospital admission. The best marker, a drop in serum bilirubin 7 days after treatment, identifies patients who have not responded to therapy, but potentially at a time when it is too late to intervene with other potential therapies.

Scientists and clinicians at Bristol University and University Hospitals Bristol NHS Foundation Trust have for some time been investigating the concept of steroid resistance in diseases affecting a number of organs ranging from the eye to the colon. White blood cells can be made to divide in the laboratory in response to various stimuli in a manner similar to that occurring during inflammation. The introduction of steroids will normally suppress the division of these white blood cells, but in about 30% of samples drawn from healthy individuals, this suppression fails to occur. This phenomenon of *in vitro* steroid resistance can be seen in individuals who fail to respond to steroids in otherwise steroid responsive diseases, such as ulcerative colitis. It is important to note that *in vitro* steroid resistance appears to be a stable property within an individual and remains the same whether a patient is well or suffering from a disease process.

Our research group has been investigating the concept of *in vitro* steroid resistance in liver disease for the past 3 years in work partly supported by the MCA, and presented at last year's American Association for the Study of Liver Disease meeting in Boston.

The group have studied 20 patients with severe alcoholic hepatitis. *In vitro* steroid resistance occurred in 68% of patients, compared with the 30% seen reported in other studied conditions. Of patients with *in vitro* steroid resistance, 82% died within 6 months, compared with only 21% of patients classified as sensitive to steroids. These results suggest that *in vitro* steroid resistance is a property that can be identified by a simple assay within 48 hours of admission, and could identify a group of patients at an early stage in whom steroids alone may not be enough to prevent death.

Another exciting aspect of our research is the ability, at least in the laboratory, to improve sensitivity of white cells to the effects of steroids. Although the exact mechanism that causes some individuals' white cells to be resistant to the effects of steroids is poorly understood at the present time, it is clear that some cytokines have a role to play. IL-2 is a pro-inflammatory cytokine that has been implicated in many inflammatory disease processes, including alcoholic hepatitis. It acts on receptors on the surface of some types

of white cells and causes them to divide. Treating isolated white cells with IL-2 can render them steroid-resistant, demonstrating the complexity of the roles of such cytokines in disease states.

IL-2 receptor antibodies are able to block the effects of IL-2 and have been used with varying success in several trials as steroid sensitisers. In one small-scale study, IL-2 receptor blockers were able to improve the outcome of patients with severe inflammatory bowel disease which was resistant to conventional steroid treatment. Our research team have shown that the same reversal of steroid resistance can be seen in the laboratory using cells from patients with severe alcoholic hepatitis. Of the patients who had steroid-resistant white cells, 91% demonstrated improved sensitivity to steroids when treated with IL-2 blocking antibodies. If this effect were to be reproduced *in vivo*, it could potentially lead to improved survival in steroid-resistant alcoholic hepatitis patients, and this is to be the focus of ongoing work. Our group hope, with time, to understand the cellular and genetic mechanisms that regulate steroid sensitivity in liver diseases such as autoimmune hepatitis and primary biliary cirrhosis, as well as alcoholic hepatitis. A better understanding of these processes could lead to strategies to improve the effectiveness of steroid treatments, resulting in

lower doses and consequently reduced side effects.

Further reading

di Mambro AJ, Parker R, McCune A *et al.* *In vitro* steroid resistance in severe alcoholic hepatitis predicts treatment response and outcome. *Hepatology* 2009;50(4) Suppl A638.

Creed TJ *et al.* Basiliximab (anti-CD25) in combination with steroids may be an effective new treatment for steroid-resistant ulcerative colitis. *Aliment Pharmacol Ther* 2003;18:65-75.

Hearing SD, Norman M, Probert CSJ *et al.* Predicting therapeutic outcome in severe ulcerative colitis by measuring *in vitro* steroid sensitivity of proliferating peripheral blood lymphocytes. *Gut* 1999;45:382-8.

New edition: *Alcohol and Health*

The new edition of *Alcohol and Health* is now available from the MCA office. It is expanded and improved, and many thanks go to Dr Marsha Morgan and Dr Bruce Ritson and their colleagues for producing such an excellent publication.

General Election 2010

The MCA has always attempted to remain an apolitical organisation, but it is inevitable that during this present epidemic of alcoholic excess, opinions expressed in these columns lend strong support towards initiatives proposed to reduce the great harm incurred on the health of this nation by these excesses. These views are largely basic common sense. The election campaign was dominated by the introduction of televised party leader debates, in which binge drinking was barely mentioned. Nevertheless, commensurate with the campaign, the BBC's *Today* programme did feature a report by John Humphrys concerning the issue of binge drinking in Cardiff on Friday and Saturday nights. His report in the *Sunday Telegraph* on 18 April¹ graphically repeated what had been reported on the radio. It is easy to comment that there was nothing that we did not already know. However, perhaps the timing was helpful, if only to re-emphasise the size of the problem to the electorate. Cuts in spending are now inevitable. A reduction in what can only be construed as self-inflicted injuries due to alcoholic excess would contribute to savings in the DH budget. In the meantime, we remain grateful for the efforts of Professor Jonathan Shepherd and his co-workers for striving to minimise alcohol-induced casualties in the Welsh capital and elsewhere.

References

- 1 Humphrys J. Binge-drinking. What happened to our sense of shame? *Sunday Telegraph* 18 April 2010.



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The Medical Council on Alcohol is a small national charity committed to improving the medical understanding of alcohol-related problems

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