Alcohol consumption during adolescence linked to reduced grey matter volumes

Chronic excessive alcohol use in adolescence may lead to neuronal loss and volumetric changes in the brain. A longitudinal study by a team from Finland compared the grey matter volumes of 35 heavy-drinking adolescents without an alcohol use disorder and 27 light-drinking controls (https://doi.org/10.1111/add.13697).

Participants were followed up using questionnaires at three time points over 10 years, with magnetic resonance imaging conducted at the last point.

Grey matter volumes were significantly smaller among heavy-drinking participants in the bilateral anterior cingulate cortex, right orbitofrontal and frontopolar cortex, right superior temporal gyrus and right insular cortex compared to the control group ($P < 0.05$). The researchers concluded that excessive alcohol use during adolescence seems to be associated with abnormal development of the brain grey matter.

Therapeutic hypothermia beneficial for adults with traumatic head injury but not children

Researchers looked at around 3100 cases of traumatic brain injury in adults and around 450 cases in children (https://doi.org/10.1097/CCM.0000000000002205). They found that cooling the brain to 33°C for 72 hours, and then allowing the patient to return to their normal temperature of 37°C at their natural speed is the most effective treatment for adults.

However, Professor Pankaj Sharma, Director of the Institute of Cardiovascular Research at Royal Holloway, highlighted that: 'whilst cooling adults is effective at providing the best possible outcome, cooling children can prove fatal. In children between the ages of 3 months and 18 years, cooling provoked a 66% increase in mortality.'

Impact of hepatitis C infection in haemodialysis patients is underestimated, finds international study

Sue Lyon

In haemodialysis patients, hepatitis C virus infection is associated with greater risk of death, hospitalization, anaemia and impaired quality of life. Despite these adverse outcomes, few haemodialysis patients are currently treated.

These are the latest findings from the Dialysis Outcomes and Practice Patterns Study (Goodkin et al, 2016), a prospective, observational, cohort study involving haemodialysis patients from more than 20 countries including the UK. Commenting on the results of the study, lead author Dr David Goodkin, from Ann Arbor, Michigan, USA, said: 'Our study also reaffirms that hepatitis C virus infection among patients on haemodialysis does not result in notable elevation of serum transaminase concentrations. For this reason, clinicians may not realize that their patients are suffering from severe liver damage and the patients are burdened by many consequences, including increased risk of death. Our data provide a rationale for treatment of greater numbers of patients.'

The study included 76 689 adult haemodialysis patients enrolled between 1996 and 2015. In the 7.5% of patients who were hepatitis C virus positive at enrolment, mean concentrations of alanine aminotransferase and aspartate aminotransferase were respectively 22.6 U/litre and 21.8 U/litre. After adjusting for age, sex, ethnicity, years on dialysis, comorbidities including hepatitis B infection, and serum albumin, phosphorus and creatinine concentrations, hazard ratios over a median follow up of 1.4 years for hepatitis C virus-positive *vs* hepatitis C virus-negative patients were 1.12 (95% confidence interval (CI) 1.05–1.20) for all-cause mortality, 5.90 (95% CI 3.67–9.50) for hepatic-related mortality, 1.09 (95% CI 1.04–1.13) for all-cause hospitalization, and 4.40 (95% CI 3.14–6.15) for hepatic-related hospitalization.

Dr David A Goodkin, Arbor Research Collaborative for Health, Ann Arbor, Michigan

Compared with hepatitis C virus-negative patients, in hepatitis C virus-positive patients the incidence of haemoglobin <8.5 g/dl was 1.12 (1.03–1.21) and the adjusted hazard ratio for transfusion was 1.36 (1.20–1.55). In addition, hepatitis C virus-positive patients had significantly worse quality of life scores on the Kidney Disease Quality of Life (KDQOL-36) instrument for physical function, pain, vitality, mental health, depression, pruritus and anorexia.

Only 1.5% of hepatitis C virus-positive patients received antiviral medication despite the availability of highly effective oral direct-acting antiviral drug combinations. In the phase 3 C-SURFER trial, for example, treatment with elbasvir-grazoprevir achieved sustained virological response rates of 99% at 12 weeks, with adverse events similar to those reported for placebo in patients with hepatitis C virus genotype 1 and estimated glomerular filtration rate <30 ml/min/1.73^2.

Hepatitis C virus infection increases mortality in dialysis patients, and has also been associated with reduced patient and graft survival following kidney transplantation. The risk of nosocomial hepatitis C virus infection has fallen in haemodialysis patients, largely as a result of measures to prevent transmission of blood-borne viruses, but hepatitis C virus prevalence remains higher than in the general population. There is increasing evidence that hepatitis C virus is itself an independent risk factor for kidney disease (most often glomerular disease), via direct cytopathic effects and the host's immune response to the virus.

The European Renal Association-European Dialysis and Transplant Association recommends that hepatitis C virus-positive haemodialysis patients should be considered for antiviral therapy regardless of the degree of liver fibrosis and whether or not they are candidates for renal transplantation.

Goodkin DA, Bieber B, Jadoul M, Martin P, Kanda E, Pisoni RL (2016) Mortality, hospitalization, and quality of life among patients with hepatitis C infection on hemodialysis. *Clin J Am Soc Nephrol* https://doi.org/10.2215/CJN.07940716

Intratympanic methylprednisolone *vs* gentamicin in patients with unilateral Ménière's disease

A double-blind comparative effectiveness trial was undertaken to assess whether intratympanic administration of methylprednisolone reduces vertigo compared with gentamicin (Patel et al, 2016). Intratympanic gentamicin, the standard treatment for refractory Ménière's disease, reduces vertigo, but damages vestibular function and can worsen hearing.

Professor Adolfo M Bronstein, Professor of Clinical Neuro-otology and Consultant Neurologist, Imperial College London, Charing Cross Hospital, London

A total of 60 patients aged 18–70 years with refractory unilateral Ménière's disease were enrolled at Charing Cross Hospital, London, and Leicester Royal Infirmary, Leicester. Patients were randomly assigned to two intratympanic methylprednisolone (62·5 mg/ml) or gentamicin (40 mg/ml) injections given 2 weeks apart, and were followed up for 2 years. The primary outcome was vertigo frequency over the final 6 months (18–24 months after injection) compared with the 6 months before the first injection.

The mean number of vertigo attacks in the final 6 months compared with the 6 months before the first injection decreased from 19·9 (standard deviation 16·7) to 2·5 (5·8) in the gentamicin group (87% reduction) and from 16·4 (12·5) to 1·6 (3·4) in the methylprednisolone group (90% reduction; mean difference −0·9, 95% confidence interval −3·4 to 1·6).

The authors concluded that methylprednisolone injections are a non-ablative, effective treatment for refractory Ménière's disease. The choice between methylprednisolone and gentamicin should be made based on clinical knowledge and patient circumstances.

Commenting on the results, Professor Adolfo Bronstein said: 'we now have good evidence that non-destructive, steroid injections are at least as good as gentamicin and possibly superior for speech discrimination outcomes. The challenge for the future is to establish whether steroid injections in patients with early Meniere's disease might prevent them developing aggressive phases of the disease.'

Patel M, Agarwal K, Arshad Q et al (2016) Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's disease: a randomised, double-blind, comparative effectiveness trial. *Lancet* **388**(10061): 2753–2762. https://doi.org/10.1016/S0140-6736(16)31461-1

Mechanisms discovered that help *Candida albicans* mask itself from detection by immune system

Candida albicans can be deadly when it takes advantage of the weakened immune systems of cancer or transplant patients. In a new study (Ballou et al, 2016), researchers have revealed ways in which the fungus can 'hide' from the human immune system.

The immune system normally detects *C. albicans* by interacting with specific molecules on its cell surface and then killing the fungal invader. Meanwhile, when the fungus senses lactic acid, it changes its cell surface to make it more difficult for the immune system to detect and kill it.

'We've discovered that this fungus is a moving target for our immune defences. It is very good at adapting to the environments within us and, through evolution, it has developed new ways to avoid being detected by our defences', said Professor Al Brown from the Aberdeen Fungal Group. 'The fungus is playing a deadly game of hide-and-seek.'

He continued: '...*Candida* can be a major health concern for some hospitalised patients. So it is important to work out how this fungus survives inside us so that we can develop ways to tip the balance back in favour of the patient.'

Ballou ER, Avelar GM, Childers DS et al (2016) Lactate signalling regulates fungal β-glucan masking and immune evasion. *Nat Microbiol* **2**: 16238. http://dx.doi.org/10.1038/nmicrobiol.2016.238

Lung function decline accelerates in menopausal women

Menopausal women appear to experience an accelerated decline in lung function. European researchers report that both forced vital capacity and forced expiratory volume in 1 second declined in women going through the menopausal transition and after menopause beyond what would be expected through normal aging (https://doi.org/10.1164/rccm.201605-0968OC).

New oral treatment for rheumatoid arthritis

The European Medicines Agency has recommended granting a marketing authorisation for Olumiant (baricitinib) for the treatment of adults with moderate to severe active rheumatoid arthritis who have not responded adequately to, or cannot tolerate one or more disease-modifying anti-rheumatic drugs. Baricitinib, which is taken orally, can be used on its own or in combination with methotrexate, and blocks the action of Janus kinases.

Viruses may target men and women differently

Viral infections can evolve to affect men and women differently and become more virulent in men (https://doi.org/10.1038/ncomms13849). Differences in the transmission routes that the sexes provide can result in evolution favouring pathogens with sex-specific virulence.

Incidence of Alzheimer's disease varies with sex, race and statin use

An American study has analysed the association between statin exposure and Alzheimer's disease incidence among Medicare beneficiaries (Zissimopoulos et al, 2016).

The medical and pharmacy claims of a sample of Medicare beneficiaries from 2006 to 2013 were examined, and rates of Alzheimer's disease diagnosis compared for 399 979 statin users 65 years of age or older with high or low exposure to statins and with drug molecules for people of different race or ethnicity. The main outcome was incident diagnosis of Alzheimer's disease.

High *vs* low exposure to statins was associated with a lower incidence of Alzheimer's disease for women and men respectively. The reduction in Alzheimer's disease risk varied across statin molecules, sex, and race or ethnicity. Clinical trials that include racial and ethnic groups are needed to confirm these findings. Because statins may affect Alzheimer's disease risk, physicians should consider which statin is prescribed to each patient.

Zissimopoulos JM, Barthold D, Brinton RD, Joyce G (2016) Sex and race differences in the association between statin use and the incidence of Alzheimer disease. *JAMA Neurol* https://doi.org/10.1001/jamaneurol.2016.3783

The geography of imported malaria to non-endemic countries: a meta-analysis

Malaria remains a problem for many countries classified as malaria free through cases imported from endemic regions. Imported cases to non-endemic countries often result in delays in diagnosis, are expensive to treat, and can cause secondary local transmission. The movement of malaria in endemic countries has also contributed to the spread of drug resistance and threatens long-term eradication goals.

A meta-analysis studied the database of publicly available nationally reported statistics on imported malaria in the past 10 years, covering more than 50 000 individual cases (Tatem et al, 2017). They obtained data from 40 non-endemic countries and recorded the geographical variations.

Infection movements were strongly skewed towards a small number of high-traffic routes between 2005 and 2015, with the west Africa region accounting for 56% (13 947/24 941) of all imported cases to non-endemic countries with a reported travel destination, and France and the UK receiving the highest number of cases, with more than 4000 reported cases per year on average. Countries strongly linked by movements of imported cases are grouped by historical, language and travel ties.

The architecture of the air network, historical ties, demographics of travellers, and malaria endemicity contribute to highly heterogeneous patterns of numbers, routes and species compositions of parasites transported. Malaria control altering local transmission, and the threat of drug resistance, understanding these patterns and their drivers is increasing in importance.

Lead author Professor Andrew Tatem, from the University of Southampton, emphasized: 'Despite malaria being prevalent in the UK just a century ago, the disease is sometimes forgotten here – but with the continuing rise of global travel, malaria will continue to be seen by clinicians all over the country. Nearly 2000 cases are diagnosed each year in the UK from people infected overseas and these will continue to pose challenges for diagnosis, management and treatment, with malaria remaining an infrequently encountered disease for many clinicians.'

Professor Andrew J Tatem, Professor within Geography and Environment, University of Southampton, Southampton

Tatem AJ, Jia P, Ordanovich D et al (2017) The geography of imported malaria to non-endemic countries: a meta-analysis of nationally reported statistics. *Lancet Infect Dis* **17**(1): 98–107. https://doi.org/10.1016/S1473-3099(16)30326-7

Multidrug-resistant tuberculosis infection higher in European migrants

Multidrug-resistant tuberculosis is widespread globally with almost half a million cases documented in 2014. Although rare in European countries, the current migrant crisis makes multidrug-resistant tuberculosis an important and urgent public health priority.

A study by a Europe-wide team has found that the rate of infection with multidrug-resistant tuberculosis is higher among migrants than in the general population, particularly in those born outside Europe and in those forced to leave their home country as asylum seekers and refugees.

The data reviewed by Hargreaves et al (2016) show that 100% of the multidrug-resistant tuberculosis cases diagnosed in Austria, The Netherlands and Norway occurred in migrants to those countries. A high proportion of multidrug-resistant tuberculosis cases were also apparent in migrants to other European states – 90% in the UK, 89% in France, 87% in Italy and 94% in Germany.

Migrants are at higher risk of contracting multidrug-resistant tuberculosis both in their country of origin, because of the breakdown of their own health-care system, and after arriving in Europe, because of destitution, homelessness, overcrowding in refugee camps or incarceration. A significant proportion of multidrug-resistant tuberculosis cases in migrants result from reactivation of latent infection.

Screening, diagnosis and treatment is available but is rarely accessed by migrants because of restrictions set by health-care systems or fear of repatriation on the part of the migrants.

Hargreaves S, Lönnroth K, Nellums LB, Olaru ID, Nathavitharana RR, Norredam M, Friedland JS (2016) Multidrug-resistant tuberculosis and migration to Europe. *Clin Microbiol Infect* https://doi.org/10.1016/j.cmi.2016.09.009

Genome-wide association studies identify four genes linked to abdominal aortic aneurysm

A 10-year project looked at 10 000 people worldwide and found those who had suffered an abdominal aortic aneurysm had four genes in common (Jones et al, 2016). As well as the UK, the research involved institutions from New Zealand, South Africa, Poland, Belgium, The Netherlands, Iceland, Australia, Denmark, Italy, Saudi Arabia, Estonia, Germany, Sweden and the USA.

It is hoped that the findings could help doctors understand more about the condition, which can lead to fatal internal bleeding if left untreated.

Professor Matt Bown, Vascular Surgeon, University of Leicester and the NIHR Leicester Cardiovascular Biomedical Research Unit and Honorary Consultant Vascular Surgeon, University Hospitals of Leicester NHS Trust, Leicester

Professor Matt Bown, a vascular surgeon from the University of Leicester and the NIHR Leicester Cardiovascular Biomedical Research Unit and Honorary Consultant Vascular Surgeon, University Hospitals of Leicester NHS Trust, said: 'Abdominal aortic aneurysm commonly affects the older population and can only be treated by surgery.

'Early detection is key to this condition which, if left untreated, can become a ticking time bomb for patients. Thousands of people die from burst abdominal aortic aneurysms each year yet about one in five men do not attend their free screening appointments so we can't detect if there may be a problem.

Professor Bown concluded: 'The discovery of the four genes, which is the culmination of more than a decade of a global research effort, could help us determine those at risk much earlier. If we are able to do this, then we could potentially save thousands of lives.'

A new research programme, funded by the British Heart Foundation, will now investigate whether the four common genes affect the speed at which the abdominal aortic aneurysms grow.

Jones GT, Tromp G, Kuivaniemi H et al (2016) Meta-analysis of genome-wide association studies for abdominal aortic aneurysm identifies four new disease-specific risk loci. *Circ Res* https://doi.org/10.1161/CIRCRESAHA.116.308765

Alternating high and low testosterone levels 'shocks' prostate cancer cells to death, early findings show

A strategy of alternately flooding and starving the body of testosterone is producing good results in patients who have metastatic prostate cancer that is resistant to treatment by chemical or surgical castration, according to findings from a phase II study (https://clinicaltrials.gov/ct2/show/NCT02090114).

In a presentation at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, researchers reported that results from 47 men who have completed at least three cycles of bipolar androgen therapy showed that the strategy was safe and effective.

Prostate-specific antigen levels fell in the majority of the men, tumours shrank in some men, in several the disease did not progress and this included some whose disease continued to be stable for more than a year. The researchers are planning to treat 60 men in total.

Professor Sam Denmeade, professor of oncology at Johns Hopkins University School of Medicine, Baltimore, USA, told the symposium: 'We think the results are unexpected and exciting. We are still in the early stages of figuring out how this works and how to incorporate it into the treatment paradigm for prostate cancer.' He added: 'this is still experimental. In particular, this therapy should only be given to men who are asymptomatic.'

Further defining influence of gender and suicide

Figures released by the Office for National Statistics (2016) show that more women took their own lives in 2015 than at any time in the previous decade. The figure for the UK as a whole was slightly up on 2014, rising from 6122 to 6188. There was a slight decrease in the number of men dying by suicide, but men are still three times more likely to take their own lives than women. More men under 30 years of age took their own lives than in the previous year. Middle-aged men are still at greatest risk.

Researchers at Leeds Beckett University have called for interventions aimed at preventing suicide among students to be designed separately for males and females (Dhingra et al, 2016).

The study examined potential gender differences in students' suicidal thoughts over a 2-week period, and explored the relationship between interpersonal beliefs and behaviour and suicide. Researchers sampled the views of over 1000 university students and found females had significantly higher levels of suicidal thoughts (68%) than males (54%).

Dr Katie Dhingra, Senior Lecturer in Criminological Psychology at Leeds Beckett, commented: 'Our results suggest the need to develop and provide separate interventions for males and females aimed at different factors. For men this can include helping them to engage with new, more realistic positive thinking, whilst for women strategies that target feelings of entrapment and burdensomeness may be more appropriate.'

Dhingra K, Debowska A, Boduszek D, Ali P (2016) Gender differences in risk and protective factors for resolved plans and preparations for suicide among university students. *Suicidology Online* **7**: 73–82

Office for National Statistics (2016) Suicides in the UK: 2015 registrations. www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/suicidesintheunitedkingdom/2015registrations#main-points (accessed 19 December 2016)