

# Science of the 'morning after'



**Temperance, not the order of drinks, is the way to escape the hangover**

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The affection that drinkers feel for alcohol has led many to believe that it is mixing drinks the wrong way, and not the drinking, which brings misery after a drinking session. One such is the notion that if one were to drink both wine and beer at a sitting, one should drink the beer first and the wine thereafter!

The aphorisms, "Beer before wine and you'll feel fine, wine before beer makes you feel queer", or "Wein auf Bier, das rat ich dir, Bier auf Wein, das lass sein", "Bière sur vin est venin, vin sur bière est belle manière", in different languages, even, "Grape or grain, but never the twain", or even "Blanc sur rouge, rien ne bouge, rouge sur blanc, tout fout le camp", attest that there is a correct order of drinking, and that it is universally known.

Jöran Köchling, Berit Geis Stefan Wirth and Kai O Hensel, researchers at Witten/Herdecke University in Germany and the University of Cambridge in the UK, thought it fit to carry out a rigorous trial to get to the bottom of these nostrums to keep the hangover away. The American Journal of Clinical Nutrition carries their report of the investigation, which had 90 participants, who were screened and admitted out of 272 volunteers. The task for the participants was to conform to set times of meals and sleep, and to drink either Premium Pilsner (five per cent alcohol) provided by Carlsberg or a 2015 Edelgräfer quality white wine (11.1 per cent alcohol), or both, till they were fairly drunk, over the course of the experiment. Of course, they had to report, during the course of the drinking, how drunk they were getting and how well or unwell they felt, and

again when they surfaced the next morning.

Most people who have experience of drinking alcohol also have the experience of getting drunk and facing the "morning after". The "morning after" is in stark contrast to the "evening before", and the euphoria and geniality that alcohol is known to create is replaced by fatigue, dehydration, an acid stomach, usually a headache, and most of all, tremendous dullness of the head and inability to focus.

The main cause, of course, is the high level of the alcohol in the blood stream that drinking sets up for some hours. As alcohol can pass through the blood-brain barrier, it begins to slow the functioning of brain cells. The first cells affected are those that promote caution and inhibit behaviour. The drinker hence feels free, powerful and euphoric. Brain cells that control speech and motor functions are also affected, causing slurred speech and loss of balance.

This is the effect in the brain. The rest of the body is also affected. With the high alcohol content of the bloodstream, water, which is the main content of cells, rushes out of the cells to dilute the bloodstream. There is hence continuing dehydration.

Another effect is that on the liver. The normal function of the liver is to maintain a steady level of sugar in the blood stream, pulling excess sugar out, and, more important, pumping sugar back in when sugar is low. The liver is also the main agent that extracts the alcohol from the bloodstream. While it is engaged in this function, the task of replenishing the sugar level in the blood is neglected and sugar levels fall.

Now, glucose in the blood is the source of energy for the brain cells.

When the person awakes a few hours after the drinking binge, there is still alcohol to be extracted but there is little sugar for the brain. The person hence feels blank, vacant and incoherent. There are often conditions of an acid stomach, headache and fatigue from unrestrained activity. The combination is a feeling of such discomfort and helplessness that the person often swears never again to "touch the stuff".

This lasts till the alcohol in the bloodstream is eliminated and the brain is again bathed in glucose. Except that if a person has been

imposing low glucose levels on the brain for some time, the brain adapts to the presence of alcohol. Now, when the level of alcohol drops, the brain pines for alcohol and the persons begins to crave a drink! And when the person gets that drink, he or she feels good and goes on to have a few more. Enter the alcoholic!

The paper in the journal starts by noting that alcohol-induced hangover constitutes a significant, yet understudied, global hazard and a large socio-economic burden. Whether the combination and the order of beer and wine consumption had any bearing on the intensity of the hangover was hence taken up for scientific study. If the traditional drinking formulae were found to be true, maybe drinkers could be educated to follow a pattern that would alleviate the hangover. The study consisted of participants divided into three groups. The first group drank beer, till their breath alcohol concentration (BrAC) reached 0.05 per cent. This, incidentally, is the level where "driving skills are significantly affected". They then switched to wine, till the BrAC was 0.11 per cent, which is nearly the level of "possible criminal penalties". The second group did the same, but started with wine and finished with beer. The third group drank just beer, till BrAC reached 0.11 per cent. A week later, there was the second round, where the first two groups switched the order of beer and wine, while the third group switched to wine.

Participants were asked about

their well-being at regular intervals and at the end of each intervention, they were asked to judge their perceived level of drunkenness on a scale between 0 and 10. They were then given six cc/kg body weight, each, of refrigerated water to drink, before they went to sleep, in similar conditions and under medical supervision. On awakening, and when the BrAC had returned to normal, an Acute Hangover Scale (AHS) of the participants' was computed. This was based on eight features, including perception of dizziness, nausea, stomach ache, tachycardia and loss of appetite.

The study group consisted of equal number of men and women, between the ages of 19-40, and had been formed into groups of three persons with similar age, gender, weight, height, BMI, reported alcohol consumption rate, and hangover frequency. A number of precautions were also taken to assure statistical reliability of the data and results to be derived.

The paper states that the trials do have limitations. For one, specific beers and white wine were used. Another is that there could be no "blind" trials. The results, however, the paper says, clearly debunk the idea that there could be a form of "tactical drinking". The only correlation that was found was that high levels of "perceived drunkenness" or the incidence of vomiting did not bode well for the morrow.

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PLUS POINTS

## New cancer drug



A cancer drug, which uses an unprecedented "Trojan horse" approach to destroy tumours from the inside, has shown promising results across six different forms of the disease.

UK researchers have hailed the results from early human tests of the drug, known as tisotumab vedotin, after it stopped or shrank tumours in patients with no other options left. The treatment combines a cancer-killing chemotherapy agent with an antibody, a biological molecule, which binds to markers on the surface of cancer cells and causes the drug to be drawn inside.

Not all patients responded to the treatment, but its effects lasted an average of 5.7 months, and up to 9.5 months in some people, in trials on bladder, ovarian, lung, and cervical cancers which were no longer responding to standard drugs.

"What is so exciting about this treatment is that its mechanism of action is completely novel — it acts like a Trojan horse to sneak into cancer cells and kill them from the inside," lead author professor Johann de Bono of the Institute of Cancer Research, "Our early study shows that it has the potential to treat a large number of different types of cancer, and particularly some of those with very poor survival rates."

New drugs are trialled in patients with advanced forms of cancer because there is a risk that side effects could be as toxic as the disease. However, de Bono said TV had "manageable side effects" and the drug is now moving on to larger, stage two clinical using the drug as a second-line treatment in cervical cancer.

The stage one trial involved nearly 150 patients with different types of drug-resistant cancer and its results have been published in the journal, *Lancet Oncology*.

The Independent

## ALS breakthrough



Scientists have identified new messenger molecules shuttled between cells, which could help to protect the survival of neurones — potentially leading to new treatments for motor neurone disease.

The pioneering research has discovered the role of a small molecule, which can regulate large signalling cascades and significantly improve the survival of neurones — something, which will help pave the way to identify and develop new therapies for neurodegenerative diseases.

MND, also known as Amyotrophic Lateral Sclerosis, is a devastating neurodegenerative disorder that affects the nerves — motor neurones — in the brain and spinal cord that tell your muscles what to do. The messages from these nerves gradually stop reaching the muscles, leading them to weaken, stiffen and eventually waste. The progressive disease affects a patient's ability to walk, talk, eat and breathe.

Approximately 10 per cent of MND cases are inherited but the remaining 90 per cent of MND cases are caused by complex genetic and environmental interactions which are currently not well understood — this is known as sporadic MND. The most common known genetic cause of MND is a mutation of the C9orf72 gene.

The new research, led by Laura Ferraiuolo from the University of Sheffield's Institute of Translational Neuroscience found that when the micro-RNA molecule — which can regulate large signalling cascades — is introduced to an astrocyte-motor neurone culture, the survival of neurones was significantly improved.

The micro-RNA identified in the study, called miR-494-3p, regulates genes involved in maintaining the health and strength of neurones axons. Researchers also found miR-494-3p was significantly depleted in cells derived from patients with sporadic MND.

Ferraiuolo said, "The results not only shed more light on the mechanisms of this complex disease but they hold massive potential for the identification and development of new therapies for ALS and other neurodegenerative diseases."

The research has been published in the *Journal EBioMedicine*.

# Chemical disquiet

The politics of the periodic table — who gets the credit and why

KELLING DONALD

The periodic table merges scientific inquiry, international politics, hero worship, desires for structure and desires for credit.

Formally, the modern periodic table is a systematic arrangement of the known chemical elements. The table is organised in an orderly way that shows the periodic occurrence of elements with similar chemical properties. Elements with similar chemical properties are stacked one on top of another in columns; going down each column from one row to the next the atoms of the elements get larger and heavier. Such periodic variations in the properties of elements are what Dmitri Mendeleev (1834-1907) and other scientists observed and sought to summarise in tabular and other forms.

Yet, the periodic table is not as objective as that basic description may sound. And who deserves credit for its creation is also not straightforward. I am a theoretical chemist; I apply chemical principles and mathematics to answer questions and solve problems in various areas of chemistry. I'm also fascinated by the history of science and how we assign credit and name things in science. Those interests coupled with my chemistry background have led me over the years to intersections of the political and the scientific in the emergence of the modern periodic table.

There are, for instance, nationalistic tilts to the periodic table. Two elements (francium and gallium) are named for France and one each for Japan (nihonium), Germany (germanium) and Poland (polonium). Scandinavia got scandium; the elements berkelium, darmstadtium and moscovium give three cities each a spot on the table. One Swedish village — Ytterby — has claimed four elements: erbium, terbium, ytterbium and yttrium. A number of other places and people have also snagged their little rectangles on the table too, and that, in some cases, only after serious

disputes.

### Exalting Mendeleev

Among the elements named after people is element number 101, mendelevium, which honors Mendeleev. Resisting other self-serving instincts, a group of Berkeley scientists who discovered the radioactive Md in 1955 decided to honour the Russian scientist Mendeleev for his contributions to formulating the periodic table. With the Cold War underway, however, they had to convince the Eisenhower administration to allow them to give up a spot on the table to a deceased Russian.

Why Mendeleev, though? Did he discover the periodic table? Hardly.

Mendeleev published in 1869 a paper that organised then-known elements in an authoritative, logical and systematic way, and he boldly predicted new ones. That paper was followed by others in the early 1870s that improved on the first and demonstrated the value of a deep appreciation for the periodicity in chemistry.

He, his papers and his table garnered a lot of attention and accelerated progress in our collective understanding of the elements and their relationships to each other. But the inspiration and the data that spurred Mendeleev's achievements were owed in huge ways to predecessors and contemporaries such as Amedeo Avogadro (1776-1856), Johann Wolfgang Döbereiner (1780-1849) and Stanislao Cannizzaro (1826-1910).

### Contenders

At the end of a chemical congress in Karlsruhe, Germany, in September 1860, for instance, a decisive paper by Cannizzaro on the weights of the atoms of the elements were distributed to the attendees. Mendeleev was at that meeting, and Cannizzaro's work helped him to organise his 1869 table of 63 known elements, which he arranged according to observed chemical properties and assigned atomic weights.

Cannizzaro's work was so con-



Stanislao Cannizzaro



J Lothar Meyer

vincing that another attendee of the Karlsruhe meeting, J Lothar Meyer, reported that it felt to him as if the scales fell from his eyes as he gained a new understanding of the elements.

Mendeleev's periodic chart appeared some nine years after the Karlsruhe meeting (1869), but by 1868 Alexandre-Émile de Chancourtois (1820-1886), William Odling (1829-1921), John Newlands (1837-1898) and Gustav Hinrichs (1836-1923), for example, had already served up, however technically inferior, credible attempts at periodic assemblies of the elements. Newlands had also predicted the existence of other elements.

Meyer, enlightened as he was by Cannizzaro, devised tables in the 1860s before Mendeleev's appeared. But his grand paper describing his table, which was similar to Mendeleev's in many respects, was published in 1870, some months after Mendeleev's 1869 paper. Predictably, a slowly festering dispute over priority eventually erupted between them.

The impressive imperfect Does Mendeleev deserve credit for producing a superb table for his time, for advancing an understanding of how the properties of atoms are rhythmically linked, for underlining the power of that understanding and for brave predictions that pushed chemistry forward? Indeed. But great victories can have more than one hero, and the emergence of our periodic table is one such victory.

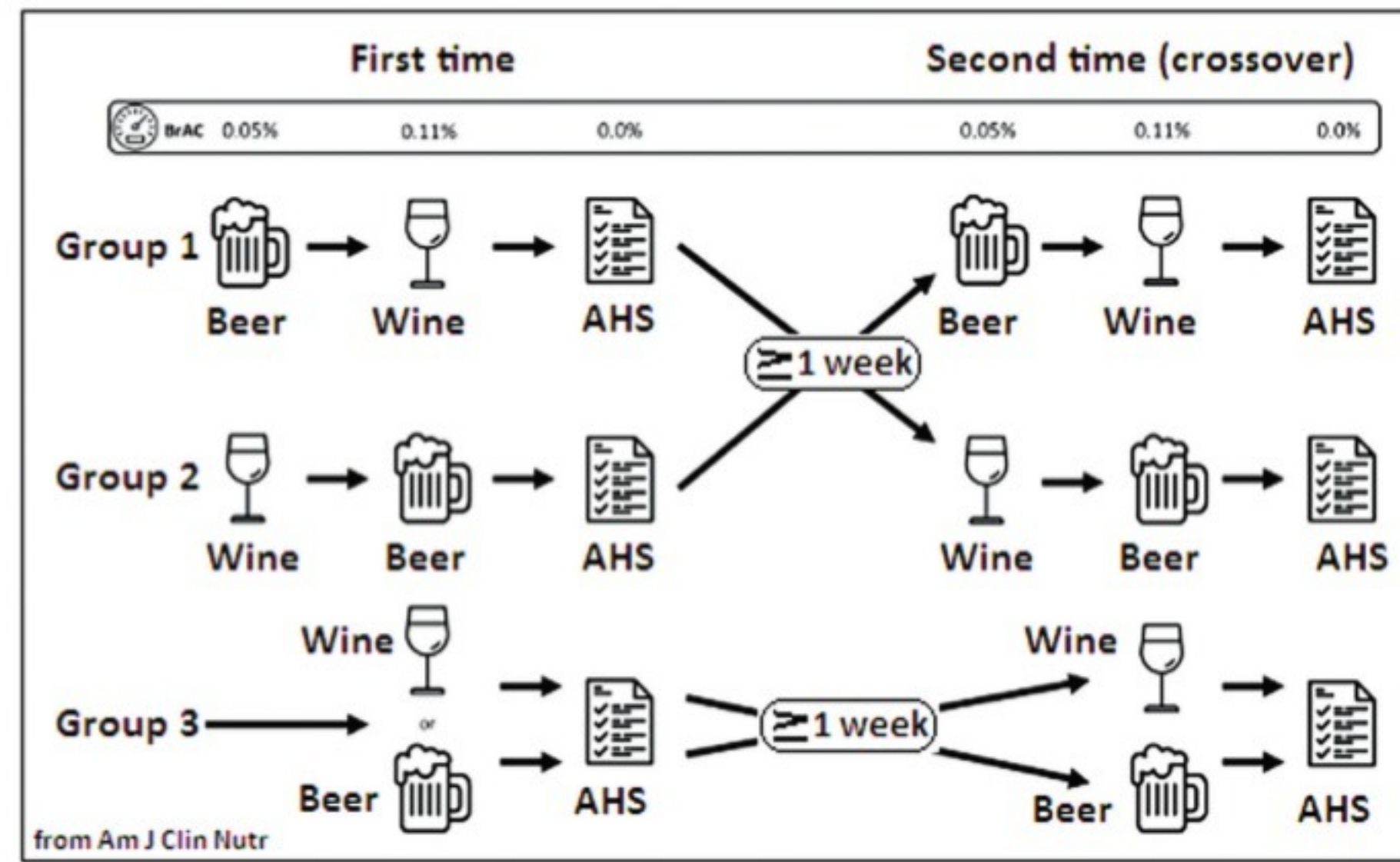
placed some elements, and his table was incomplete, even with his predictions: the group of so-called noble gases, for example, was discovered in the 1890s and was not anticipated in his papers. And general chemistry students today can readily spot other deficiencies in his 1869 table, too, based on our contemporary understanding of the nature of the elements.

In brief, Mendeleev's contribution was tremendously impressive but was also imperfect, and the value of Meyer's contributions was already sufficiently clear as to move the Royal Society of London to award both him and Mendeleev their prestigious Davy Medal in 1892 "for their discovery of the periodic relations of the atomic weights." Indeed, the joint award has been cited as evidence that what was seen by some to be especially valuable about Mendeleev's table was how it accommodated (as Meyer's also did) the elements that were known, and not so much for Mendeleev's predictions of new elements.

Was the Royal Society hoping too, through the joint award, to muffle the disquiet about priority or credit for the increasingly indispensable table? Perhaps. But if that were the intention, they failed. In science as in politics, the temptation to be simple rather than accurate can be quite strong. Scientists still say, "Mendeleev discovered the periodic table."

### Noble intentions, political interventions

Whatever one thinks of Meyer's versus Mendeleev's role in the incarnation of the table, history has not



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