

Masala

A phase 1 study gone terribly wrong...

In a phase 1 trial, BIA 10-2474, an inhibitor of fatty acid amide hydrolase, which has shown analgesic and anti-inflammatory properties in animal studies, was tested in healthy volunteers. Single doses (0.25 to 100 mg) and repeated oral doses (2.5 to 20 mg for 10 days) of the drug had been given to 84 healthy volunteers in sequential cohorts without any severe adverse effects. After this, another cohort of 8 volunteers was assigned to placebo ($n=2$) or the active drug ($n=6$) in a dose of 50 mg per day. Of the 6 healthy volunteers given the drug, 1 died with evidence of extensive neurological injury on imaging; 2 declined consent to be included in the published report; 3 of 4 other participants developed a severe, acute neurological disorder characterized by a cerebellar syndrome, amnesia, headache and altered sensorium starting from day 5 of drug intake. Although the drug was withdrawn immediately, the volunteers improved to variable degrees over the next 55 days (*N Engl J Med* 2016;**375**:1717–25).

A healthy lifestyle offsets high genetic risk of coronary artery disease

Researchers in the USA evaluated DNA sequence polymorphisms to quantify the genetic risk of coronary artery disease (CAD) in participants from three large prospective cohorts—Atherosclerosis Risk in Communities (ARIC) ($n=7814$), Women's Genome Health Study (WGHS) ($n=21\ 222$) and Malmö Diet and Cancer Study (MDCS) ($n=22\ 389$) and from the cross-sectional BiImage Study ($n=4260$). A scoring system assessed adherence to a healthy lifestyle in terms of not smoking, maintaining a healthy weight, regular physical activity and a healthy diet. Participants at the highest genetic risk of CAD had a 91% higher relative risk of coronary events compared to those with the lowest genetic risk. A favourable lifestyle reduced the risk of CAD in those at highest genetic risk by 46% and led to halving of the 10-year incidence of coronary events (*N Engl J Med* 2016;**375**:2349–58).

Reading Petrarch will keep the doctor away!

Petrarch, a 14th century Italian poet, found much to criticize in physicians. Following the great plague of the mid-14th century, he advised people not to visit doctors. A fresh interpretation of a part of his work published in the collection called *Seniles* has been presented by Dr Donaldson of the University of Edinburgh. In this writing, Petrarch describes how he heard a famous doctor say that he was convinced that of a hundred or a thousand men of the same age and habits with the same disease, between the half who followed the prescriptions of doctors and the half who followed Nature's instincts, it was clear who would improve (the latter!). Many view this as the first suggestion of the design for a randomized controlled trial (*J R Soc Med* 2016;**109**:347–53).

Brain-computer interface offers hope for patients with locked-in syndrome

Locked-in syndrome is characterized by loss of voluntary muscle contraction with intact cognitive function. For such patients, eye-tracking devices which monitor the patient's eye movements with a camera are often the only means of communication. Researchers from the Netherlands report the

use of a new brain-computer interface created by Medtronic in a 58-year-old woman with late stage amyotrophic lateral sclerosis, a type of motor neuron disease. The brain-computer interface consisted of subdural electrodes placed over the motor cortex and a subcutaneous transmitter. When the patient attempted to move the hand opposite to the side with the implanted electrodes, she could generate 'brain clicks' which were transmitted to the computer. Using this she could choose letters displayed on the computer screen and spell out words. Although it required training for 28 weeks and she could only manage to select two letters per minute, this work opens up the possibility of better communication for patients who are locked-in (*N Engl J Med* 2016;**375**:2060–6).

Vasectomy and the risk of prostate cancer

Researchers from Atlanta evaluated the risk of carcinoma of the prostate following vasectomy. In a cohort of 363 726 men in the Cancer Prevention Study II (CPS-II), mortality due to prostate cancer was not found to be associated with previous vasectomy. In a subgroup of 66 542 men from the CPS-II Nutrition cohort, vasectomy was not associated with the overall incidence of prostate cancer or with the incidence of high-grade prostate cancer. Given that data from the Health Professional Follow-Up Study published in 2014 (*J Clin Oncol* 2014;**32**:3033–8) had revealed an increased incidence of prostate cancer in men who had had a vasectomy, this is reassuring news (*J Clin Oncol* 2016;**34**:3880–5).

This will put you to sleep!

The American Heart Association has released a scientific statement on the impact of sleep duration and quality on cardiometabolic risk. The statement highlights the fact that 50 to 70 million adults in the USA suffer from a sleep disorder or report getting inadequate sleep; insomnia afflicts 5% to 15% of the population; sleep apnoea affects nearly a quarter of adults between 30 and 70 years of age. Both insomnia and obstructive sleep apnoea lead to a host of cardiovascular disorders including arrhythmias and coronary artery disease. Short sleep duration (<7 hours/night) is associated with a greater incidence of obesity, diabetes mellitus and hypertension. The statement highlights the need for 7 or more hours of sleep a night for 'optimal health' (*Circulation* 2016;**134**:e367–e386).

Anxiety about health increases the risk of ischaemic heart disease

The incidence of ischaemic heart disease was evaluated in 7052 participants in the Hordaland health study (HUSK) and correlated with data from the Cardiovascular Diseases in Norway (CVDNOR) project. The Whiteley Index was used to identify participants with health anxiety, defined as a score more than the 90th percentile. During 12 years of follow-up, ischaemic heart disease developed in 6.1% of those with health anxiety compared with 3% of those without anxiety. After adjustments for traditional cardiovascular risk factors, about 70% of the increased risk was attributed to health anxiety. Those with higher anxiety levels were at higher risk. So-called 'cardiac neurosis' could actually raise the risk of ischaemic heart disease (*BMJ Open* 2016;**6**:e012914.)!

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