#### **NEWS**



"...as a consequence of this rise in control there may be as many people now being over-treated (8%) with blood pressure medications as there are being under-treated (6%)."

Recent dramatic improvements in blood pressure control in diabetic patients is promising, but could indicate that many people are now being over treated with blood pressure medications, wasting resources and potentially causing harm to patients.

FSUITS

A paper, published in the *Archives of Internal Medicine*, looked at 977,000 Veterans Affairs patients and suggests that as many as 82% of patients are now having their blood pressure controlled and 94% are receiving appropriate blood pressure treatment. This is very encouraging news, but the paper also suggests that as a consequence of this rise in control there may be as many people now being over-treated (8%) with blood pressure medications as there are being under-treated (6%).

"We need to find better ways to measure and incentivize appropriate blood pressure management..."

The 'one-size-fits-all' approach to blood pressure lowering in diabetic patients began many years ago when blood pressure in diabetes was high across the board, however, now that the majority of diabetic patients have good control over their blood pressure, targets may need to be revisited.

"Appropriately treating blood pressure in people with diabetes is extremely important, and good blood pressure control should still be the goal to reduce risk of heart attack, stroke and other conditions," explains Eve Kerr, from Veterans Affairs Ann Arbor Healthcare System and the University of Michigan Health System (both MI, USA), and lead author on the *Archives of Internal Medicine* paper. "But just treating to a blood pressure target in all patients may result in over treating and harming some patients because their blood pressures actually fall too low," she continues. "We need to find better ways to measure and incentivize appropriate blood pressure management to make sure that patients who need aggressive treatment are getting it, and to decrease the rate of inappropriate over-treatment."

The study used electronic records of people with diabetes and high blood pressure who were treated between 2009 and 2010. In this study, appropriate blood pressure management was having either less than 140/90 mmHg or less than 150/65 mmHg; or having appropriate management of elevated blood pressure and being on three or more blood pressure medications. Potential over-treatment was defined as receiving three or more blood pressure medicines or having recent medication increases and having blood pressure that was less than 130/65 mmHg.

The blood pressure clinical action measure used in this study will be adopted by the Veteran Affairs healthcare system to motivate appropriate blood pressure management for patients based on their risks and treatment characteristics. It could also be rolled out to non-Veteran Affairs centers, but in the meantime, diabetic patients are advised to talk to their doctors about appropriate blood pressure management.

- Written by Laura McGuinness

Source: Kerr EA, Lucatorto MA, Holleman R *et al.* Monitoring performance for blood pressure management among patients with diabetes mellitus: too much of a good thing? Monitoring performance for BP management in diabetes *Arch. Intern. Med.* doi:10.1001/archinternmed.2012.2253 (2012) (Epub ahead of print).



## News & Views

### News

Journal Watch

Ask the Experts



#### NEWS & VIEWS | News



# New diagnostic test for safer, earlier detection of bone loss

A new diagnostic test to detect bone loss has been recently developed by scientists from NASA and Arizona State University (USA). The new tool measures calcium isotopes and has the potential to be safer than current methods and diagnose bone loss earlier. The technology is also hoped to have potential diagnostic applications for diseases such as osteoporosis and cancer, in which bone loss can occur in the advanced stages.

"The new tool measures calcium isotopes and has the potential to be safer than current methods and diagnose bone loss earlier."

Dual-energy x-ray absorptiometry is the current method used to detect bone loss. Ariel Anbar (Arizona State University) senior author on the study explains, "By the time these changes can be detected by x-rays, as a loss of bone density, significant damage has already occurred." The new test developed by Anbar and colleagues looks to avoid this damage by allowing diagnosis to occur at an earlier stage and at less reduced risk to the patient as it involves no exposure to radiation.

The new technique detects bone loss through the analysis of calcium isotopes that naturally occur in urine. Through assessing changes in calcium isotope ratios in urine, the test aims to detect when disease is disrupting the natural balance of bone formation and destruction. These small changes in calcium isotopes are measured using mass spectrometry methods. In the recent study, a dozen healthy participants were confined to bed rest for 30 days to measure the effect of 'skeletal unloading', a condition where extended rest causes bone deterioration similar to that of osteoporosis patients and astronauts. The new test was reported to detect bone loss after as little as just 1 week of bed rest - much sooner that would be detectable by the conventional x-ray method.

Following on from the study, the researchers are now looking to the potential clinical applications of the test, Anbar comments, "This is a 'proof-of-concept' paper. We showed that the concept works as expected in healthy people in a well-defined experiment. The next step is to see if it works as expected in patients with bone-altering diseases. That would open the door to clinical applications." Furthermore, the authors recognize that the potential uses for the test extend beyond bone as many diseases cause subtle changes in concentrations of elements or element isotope abundances. The potential to therefore develop 'biosignatures' for disease, based around these changes, could be a future direction for disease diagnostics.

#### Written by Jenaid Rees

Source: Arizona State University press release 'Earlier detection of bone loss may be in future': https:// asunews.asu.edu/20120528\_isotopes



### New microfluidics test holds promise for improved diagnostics of latent tuberculosis

Researchers at the University of California Davis (CA, USA) have recently developed a new test with the ability to diagnose latent tuberculosis. The test is based on microfluidic chip technology and holds potential for latent tuberculosis diagnosis that is reliable, faster and more affordable than is currently achievable using available technologies.

Approximately a third of the world's population is infected with latent tuberculosis, although the risk of becoming ill with tuberculosis is only 10%. People with compromised immune systems, such as those suffering from HIV, carry a much higher risk of developing full-blown tuberculosis, and the disease is estimated to cause a quarter of all deaths among people living with HIV. At present, tests for latent tuberculosis work through detecting IFN- $\gamma$ , a chemical made by the immune



#### News | NEWS & VIEWS

system. However, current commercially available tests can only be used once and must be sent to a lab.

The University of California Davis researchers have built upon current methods to devise their novel technique. The scientists coated a gold wafer with pieces of ssDNA complementary to IFN- $\gamma$ , then mounted the wafer in a chip with channels for blood samples. An electrical signal is triggered if IFN- $\gamma$  is present in a blood sample, which can be read by a clinician. Ying Liu of the University of California Davis concludes, "If you see that the IFN- $\gamma$  level is high, you can diagnose latent tuberculosis."

The University of California Davis researchers have already tested blood samples from patients in China and the USA and have future plans to integrate the electronic readout and microfluidic sensor onto

### Stem cell therapy approved for treatment of graftversus-host disease in children

Prochymal<sup>®</sup> (Osiris Therapeutics, Inc., MD, USA) has become the first stem cell therapy to receive regulatory approval after being authorized in Canada for the treatment of refractory acute graft-versus-host disease (GVHD) in children.

The approval by the Canadian regulatory body, Health Canada, was given upon the recommendation of an independent expert advisory panel, which took into account positive trial results demonstrating a clinically meaningful response in 61–64% of patients as well as a statistically significant improved survival in comparison with a historical control population.

A condition of the approval, which was made under Health Canada's Notice of Compliance with Conditions policy, is that the sponsor must carry out trials to confirm the clinical benefit of the drug. Osiris has indicated that Prochymal will be further evaluated in a case-matched study and has urged that all patients receiving the drug be enrolled in a registry so that its long-term efficacy can be monitored.

In addition to advancing the use of stem cell therapy in clinical practice, the approval of Prochymal is also significant for representing the first time an approved therapy for GVHD has become available to clinicians. Acute GVHD is a serious complication of bone marrow or stem cell transplantation that causes damage to the skin, the GI tract and the liver, in particular, and is fatal in up to 80% of cases. The current first-line therapy for the condition is immunosuppression with steroids; however, this is effective in only 30–50% of patients. Prochymal is intended for use in those cases where treatment with steroids has failed.

Prochymal is expected to be commercially available in Canada later in 2012, and is available in several other countries, including the USA, under an Expanded Access Program, which offers access outside the clinical trial setting for emergency or compassionate use.

Prochymal is the proprietary name of remestemcel-L, a formulation of mesenchymal stem cells derived from healthy adult donors and expanded *ex vivo*. Described by Andrew Daly (University of Calgary, Canada, and Principal Investigator in the Phase III clinical program for Prochymal) as "an off-the-shelf stem cell therapy," Prochymal can be frozen at the point of use and is administered intravenously, without the requirement to type or immunosuppress the patient.

#### - Written by Sarah Stokes

Sources: Osiris press release: www.osiris.com/ pdf/2012-05-17%20Health%20Canada%20Release.pdf; Medical News Today news story: www.medicalnewstoday.com/articles/245618.php a single chip. In addition, a patent application has been filed and the researchers will look to commercialize the test after US FDA approval.

#### - Written by Jenaid Rees

Sources: University of California Davis press release: www.news.ucdavis.edu/search/news\_detail.lasso<sup>-</sup> ?id=10260; WHO tuberculosis factsheet: www.who.int/ mediacentre/factsheets/fs104/en/







# Potential new drug treatment identified for amebiasis

#### Group achieve FDA approval for 'orphan drug' status.

Researchers from the University of California San Diego and the University of California San Francisco (CA, USA) have announced that auranofin has been granted orphan drug status by the US FDA after a series of tests revealed it could be used to treat amebiasis.

Amebiasis is caused by the protozoan *Entamoeba histolytica* and is the fourth leading cause of death due to protozoans worldwide. It has been associated with up to 70,000 annual deaths worldwide. Amebiasis is a gastrointestinal infection that can cause dehydration, diarrhea and dysentery. It mainly spreads through water and food that has been contaminated and children are especially vulnerable to the disease. The current treatment using the drug metronidazole has been reported as being increasingly ineffective in recent years, highlighting the need to find new treatments for amebiasis.

The potential to use auranofin was discovered following a high-throughput

screen. Auranofin had previously been used as a drug to treat rheumatoid arthritis. The work carried out by the group indicated that auranofin could be up to ten-times more potent than metronidazole; potentially leading the way to a lower dose level or even reduced administration frequency.

"The current treatment using the drug metronidazole has been reported as being increasingly ineffective in recent years, highlighting the need to find new treatments for amebiasis."

One of the authors, James McKerrow from the University of California San Francisco, explained the reasoning behind the approach taken: "When we're looking for new treatments for the developing world, we start with drugs that have already been approved." Anjan Debnath also from the University of California San Francisco commented on the prospects for the drug: "This is a drug that you can find in every country. Based on the dosage we're seeing in the lab, this treatment could be sold at about \$2.50 per dose, or lower. The cost savings could make a big difference to the people who need it the most."

Another author, Sharon Reed, from the University of California San Diego, emphasized the potential for the drug given its FDA approval: "Because auranofin has already been approved by the FDA for use in humans, we can save years of expensive development. This new use of an old drug represents a promising therapy for a major health threat, and highlights how research funded by the National Institutes of Health can benefit people around the world."

- Written by Andreas Hadjivasiliou

Source: Debnath A, Parsonage D, Andrade RM *et al.* A high-throughput drug screen for *Entamoeba histolytica* identifies a new lead and target. *Nat Med.* doi:10.1038/ nm.2758 (2012) (Epub ahead of print).



# Pediatric Crohn's patients may benefit from determination of bone age

A study published recently in *Inflammatory Bowel Disease* by a group from the University of California San Francisco (CA, USA) has suggested that measuring bone age should become standard practice in pediatric patients suffering from Crohn's disease. The aim of the measurements would be to improve treatment and interpret growth status.

Children suffering from Crohn's disease are often faced with complications including delayed puberty and impaired growth. Growth status is often one of the criteria for determining treatment options in these patients. In fact, diagnosis in many children relies on identifying lack of growth as the primary symptom of Crohn's. This study used detailed measurements for bone age using a left hand/wrist x-ray to determine bone age.

Lead researcher Neera Gupta from the University of California San Francisco summarized the findings of the study: "Not only is bone age helpful in predicting a child's remaining growth potential, our study demonstrates that bone age is necessary to correctly interpret a patient's growth status in pediatric Crohn's disease."

Commenting on the specific results of the study, Gupta stated: "One of our findings that surprised me was that 41% of our patients had bone age-Z scores that

#### News | NEWS & VIEWS

were less than 2. I did not expect that such a large proportion of patients would have this degree of delay."

Gupta highlighted her belief that changes were needed to the diagnostic aspect in pediatric patients: "It is important to know that active inflammation may be present even without classic intestinal symptoms such as abdominal pain, rectal bleeding or diarrhea. Poor growth may be the only sign of active disease. Including the x-ray as part of routine care allows a more clinically meaningful interpretation of statural growth and therefore enables us to improve our treatment recommendations."

The need for further work was also mentioned by Gupta, who said: "We need further studies to understand the effects of disease activity on bone age advancement and to determine which patients require more frequent monitoring of bone age."

#### - Written by Andreas Hadjivasiliou

Source: Gupta N, Lustig RH, Kohn MA, Vittinghoff E. Determination of bone age in pediatric patients with Crohn's disease should become part of routine care. *Inflamm. Bowel Dis.* doi:10.1002/ibd.22979. (2012) (Epub ahead of print).



## Ketamine as new treatment for bipolar depression

Antidepressants are the usual treatment for bipolar depression; however, they are not always effective and a lag period can occur between start of drug intake and onset of treatment action. A recent study published in Biological Psychiatry by Carlos Zarate (National Institute of Mental Health, MA, USA) and colleagues found that ketamine could treat bipolar depression. The placebo-controlled crossover study randomized 15 subjects with bipolar depression DSM-IV I and II to a single intravenous infusion of either placebo or ketamine 0.5 mg/kg on 2 days spaced 2 weeks apart. The patients maintained their usual therapy of lithium or valproate. The primary outcome measure was Montgomery Asberg Depression Rating Scale baseline 10, 80, 110 and 230 min after infusions and at 1, 2, 3, 7, 10 and 14 days after infusion, which was used to rate symptoms and overall depression.

Depressive, as well as suicidal, symptoms were significantly reduced in the subjects receiving ketamine compared with placebo and the effect was maintained for up to 3 days. The response rate to ketamine was 79% and the response to placebo was 0%.

Zarate commented, "We think that these findings are of true importance given that we only have a few treatments approved for acute bipolar depression, and none of them have this rapid onset of action; they usually take weeks or longer to have comparable antidepressant effects as ketamine does." The study replicated previous findings, which is important for confirmation of the response seen.

Ketamine is a *N*-methyl-D-aspartate (NMDA) receptor antagonist and the study conformed that blocking the NMDA pathway is successful in reducing depressive symptoms and gives hope that new treatments can be explored in this area.

#### - Written By Claire Attwood

Source: Zarate CA, Brutsche NE, Ibrahim L. Replication of ketamine's antidepressant efficacy in bipolar depression: a randomized controlled add-on trial. *Biol. Psychiatry* 71(11) 939–946 (2012).



The News highlights some of the most important events and research. If you have newsworthy information, please contact: Laura McGuinness, Commissioning Editor, *Clinical Practice* Future Medicine Ltd, Unitec House, 2 Albert Place, London, N3 1QB, UK Tel.: +44 (0)20 8371 6090; Fax: +44 (0)20 8343 2313; I.mcguinness@futuremedicine.com

