

New findings have backed up a 4-year clinical trial to prove the efficacy of ibuprofen in slowing the decline of lung function.

## Ibuprofen shows a slow in the decline of lung function in cystic fibrosis patients

Observational study data has revealed that children and adolescents with cystic fibrosis (CF) who are treated with ibuprofen have slower rates of FEV<sub>1</sub> decline than those not treated with the nonsteroidal anti-inflammatory drug.

These findings back up a 4-year clinical trial indicating that ibuprofen may be effective in reducing the rate of lung function decline. This study used high-dose ibuprofen in a 4-year controlled trial to highlight the effectiveness of ibuprofen in a large group of patients treated clinically with this therapy. Inflammation contributes to lung damage in CF, shortening the survival of patients with the disease. FEV<sub>1</sub> decline predicts survival in CF.

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Michael Konstan, lead author of the observational study, explained "To examine whether high-dose ibuprofen is as effective when it is used in the clinical setting as it was under the highly controlled conditions of the original trial, we turned to the Cystic Fibrosis Foundation Patient Registry, which records

information on all consenting patients with CF, monitored at US CF centers,"

Multilevel repeated-measures mixed-regression models were used to estimate rates of decline, adjusting for characteristics and therapies that influenced FEV<sub>1</sub> decline, such as the recently introduced treatments inhaled tobramycin and dornase alfa. Adverse effects were compared among those treated versus nontreated patients.

Researchers studied the rate of decline in FEV<sub>1</sub> percentage and predictions over 2–7 years. A total of 10,325 patients aged between 6–17 years with a predicted baseline FEV<sub>1</sub> of less than 60% were treated with either ibuprofen or placebo.

Results confirmed that a significantly less rapid decline in lung function was seen in the patients treated with ibuprofen. Predicted values showed that over a 5-year period lung function would decrease by -7.43 and -9.87% in treated versus nontreated patients, respectively.

Further analysis indicated that "This improvement is less than reported under clinical trial conditions but is still significant," Konstan noted.

The main side effect of ibuprofen usage in children and adolescents is gastrointestinal bleeding requiring hospitalization.

This occurred more frequently in patients treated with ibuprofen than those not, at an annual incidence of 0.37% versus 0.14%. The authors described the incidence of adverse gastrointestinal bleeding as 'rare.'

It is concluded in the *American Journal of Respiratory and Critical Care Medicine* that "Slower rates of FEV<sub>1</sub> decline are seen in children and adolescents with cystic fibrosis who are treated with ibuprofen."

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"The apparent benefits of ibuprofen therapy outweigh the small risk of gastrointestinal bleeding," Added Konstan. The study has given an insight into the possible 'real-world' clinical use of ibuprofen and its association with a slower rate of FEV<sub>1</sub> decline in children with CF. These results should lead to an increase in the use of ibuprofen among patients with CF.

Source: Konstan MW, Schluchter MD, Xue W, Davis PB: Clinical Use of ibuprofen is associated with slower FEV<sub>1</sub> decline in children with cystic fibrosis. *Am. J. Respir. Crit. Care Med.* 176, 1084-1089 (2007)

## Relief from vulvodynia with physical therapy

Women suffering from unexplained pain or discomfort in the vulva can find relief with physical therapy, according to the American Physical Therapy Association (APTA).

Vulvodynia affects an estimated 14 million women in the USA, although many women chose not to discuss the problem with their doctors due to the disorders intimate nature.

"Women who experience pelvic pain and discomfort will typically consult first with their general practitioner or gynecologist," Pamela Morrison, a physical therapist notes. "However, some doctors may not be familiar with the terms vulvodynia, vaginismus (vaginal muscle spasm with any kind of attempted penetration), or vulvar vestibulitis (vulvar pain local to the vaginal opening)."

"If we can teach women with pelvic pain – either during intercourse or all the time – just one thing, it would be for them to know their options for medical treatment and to be their own best advocates when it comes to pelvic health," added Morrison.

Morrison explains that causes for pelvic floor muscle dysfunction can include muscle pain, weakness, incoordination, spasm or result from tearing during childbirth. Therapy involving therapeutic ultrasound, electrical stimulation and biofeedback can help women to overcome this pain.

Source: The American Physical Therapy Association [Press release]

## in brief...

**A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions.**

Milano MT, Katz AW, Muhs AG *et al.*: *Cancer* [Epub ahead of print] (2007).

It is hypothesized that oligometastatic disease represents a state of potentially curable, limited metastases. Stereotactic body radiation therapy (SBRT) is an option for patients who are not able to undergo resection. This study enrolled 121 patients with detectable metastases into 2 prospective studies that used curative-intent SBRT. The 2-year overall survival (OS), progression-free survival (PFS), local control (LC), and distant control (DC) rates were 50%, 26%, 67%, and 34%, respectively. It was concluded that Oligometastatic disease is a potentially curable state of distant cancer spread.

**A long term follow-up study investigating health related quality of life and resource use in survivors of severe sepsis: comparison of recombinant human activated protein C to standard care.**

Longo CJ, Heyland DK, Fisher HN *et al.*: *Crit. Care*. 11,11(6), R128 [Epub ahead of print] (2007).

Recombinant human activated protein C (APC) therapy has been shown to reduce short-term mortality in patients with severe sepsis, this study explores the long term complications affecting health-related quality of life (HRQoL) in survivors of sepsis. An observational cohort study at nine Canadian intensive care units recruited severe sepsis patients who survived to 28 days. Patients received either APC or placebo. A total of 100 patients were enrolled. The treated group showed statistically significantly better scores for the Physical Component Score, trends towards improvements in Physical Functioning and Bodily Pain, compared to the non treated patient group.

**Adenovirus carrying TIMP-3: A potential tool for cervical cancer treatment.**

Zhang Y, Qian H, Lin C *et al.*: *Gynecol Oncol*. [Epub ahead of print] (2007).

Previous research has indicated that an important role is played by matrix metalloproteinases (MMPs) in cervical cancer progression. To investigate this role, study authors used a replication deficient adenoviral vector carrying tissue inhibitor of metalloproteinases-3 (TIMP-3); an inhibitor of all MMPs. Results of the study demonstrated that overexpression of TIMP-3 caused arrested growth of the cell lines in the G(2)/M phase as well as causing potent growth inhibition bystander effects. The researchers conclude that Ad-TIMP may have potential role in the therapeutics of cervical cancer.

**Novel biomarker helps identify high-risk ACS patients earlier**

A team of UK researchers have developed a new biomarker which will help the Identification of patients suffering from acute coronary syndrome (ACS), but who do not present any sign of myocardial damage when using the Troponin assay test.

The biomarker uses heart type fatty acid-binding protein (H-FABP) levels to identify patients presenting with ACS, who have a poor prognosis but do not show any sign of myocardial damage.

“The H-FABP test is a major advance on what we had before,” explained lead investigator Alistair Hall, from the University of Leeds, UK.

Hall's team conducted a prospective observational study in 1448 patients admitted to hospital with ACS, to test the clinical

performance of a sensitive H-FABP assay in predicting adverse prognosis. Multivariable analysis revealed that H-FABP levels were strongly predictive of outcome, with patients' relative risk for 1-year mortality rising significantly across increasing H-FABP quartiles.

“This blood test, which will cost about £10 (US\$20), could be used by ambulance crews to test people on the way to hospital. [It] will enable us to send the right people home earlier and make sure we aren't admitting people who don't need to be admitted.” Hall added.

Source: Kilcullen N, Viswanathan K, Das R *et al.*: Heart-type fatty acid-binding protein predicts long-term mortality after acute coronary syndrome and identifies high-risk patients across the range of troponin. *J. Am. Coll. Cardiol.* 50(21), 2061–2067 (2007).

**Patients suffering severe forms of migraines could be helped by genetic testing**

New research indicates that genetic testing might benefit people who suffer from a severe type of migraine. Familial (FHM) and sporadic (SHM) hemiplegic migraine are a very rare but severe form of migraine.

Previously, three genes have been shown to be associated with FHM although their function in SHM is yet to be established.

In this study, a total of 39 patients with SHM, both male and female, were systematically tested for variations in the three genes mentioned above. The scientists found sequence variants in seven of the patients in the study, with mutations in *ATPIA2* being the most common.

“Since many people with this type of migraine are initially misdiagnosed and not given the proper treatment, understanding the genetic basis of this type of

migraine may help clinicians in diagnosing and treating the problem. Most patients are initially diagnosed with epilepsy, stroke or other disorders and are treated accordingly with non-effective medications that are associated with a high risk of side effects rather than with effective agents to treat migraine.” explained study author Michel Ferrari.

“Our findings reinforce the growing evidence that familial and sporadic hemiplegic migraine along with normal migraine have some shared gene pathways. Unraveling these pathways may help to identify new treatment options,” concluded Ferrari.

Source: de Vries B, Freilinger T, Vanmolkot KR *et al.*: Systematic analysis of three FHM genes in 39 sporadic patients with hemiplegic migraine *Neurology* 69, 2170–2176 (2007).

## Ultrasound-guided percutaneous therapy relieves shoulder pain

Doctors at the 93rd Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA) have claimed that ultrasound-guided percutaneous therapy is able to relieve shoulder pain caused by calcification of the tendons.

This quick inexpensive treatment uses a simple saline lavage treatment to dissolve and rinse away the calcified tissues. The method successfully removed more than 50% of the calcium from the shoulder lesion in over 93% of cases.

“This is a quick, successful and inexpensive therapy for tendon calcification,” said Luca Sconfienza, who led the study.

This new treatment takes up to 15 minutes and can cost around US\$100. Open surgery for the same problem can require up to 2 months recovery and cost

around 50 times as much.

The technique involves an ultrasound and a 16 gauge needle which is used to guide a calcium capsule to the site, a second needle is used to introduce saline into the calcium. The water is then recovered through the second needle as it flows out of the space. The saline solution is used to dissolve the calcium which is expelled with the water.

“We don’t know why some people develop these calcifications,” added Sconfienza.

The exact cause of calcification of tendons is unknown, there appears to be no correlation between dominant arm use, or type of employment, but there is always a reduced blood supply in the affected shoulder present along with the calcification. This causes a change in the

environment in the shoulder and tendon; it is thought that this aids the build up of crystals of calcium, which in turn cause inflammation and pain in the patient leading to impaired use of the entire limb.

The study involved 990 men and 1798 women, ranging in age from 29 to 73 years. In over 70% of the cases all the calcium was removed, 23% of the patients have over 50% of the calcium removed. Only 2.1% of patients were left with unchanged calcium levels in the affect area.

“Under precise ultrasound guidance, this procedure is more effective than others in the treatment of calcific shoulder,” Dr Sconfienza said.

Source: Presentation title: Ultrasound (US)-guided percutaneous approach to the therapy of calcific tendonitis of rotator cuff. Abstract SST15-09.

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## New ablation technique successful in the treatment of Barrett’s esophagus

A new technique to treat Barrett’s esophagus (BE) has been proven to be effective and well-tolerated. The new ablation technique – Halo 360 – uses radio frequency energy to kill problem cells in the patient’s esophagus.

Esophagectomy is traditionally recommended for patients with high-grade dysplasia, but it is not a benign procedure, particularly in elderly and high-risk patients with relatively high morbidity and mortality rates.

The research was lead by George Triadafilopoulos and colleagues from the Stanford University School of Medicine in California, Ca, USA.

The team conducted symptom evaluation, endoscopy and histologic assessment, esophageal motility testing, pH monitoring on proton pump inhibitor, computerized tomography, endoscopic ultrasonography and mucosal resection for nodules on 13 BE patients. The halo technique was then carried out in combination with twice daily proton

pump therapy. Each patient was followed up every 3 months, for 12 months. If metaplasia or dysplasia were detected at follow-up, patients underwent second ablation with the Halo technique. A total of three of the patients were found to have high-grade dysplasia, four patients displayed low-grade dysplasia and six were diagnosed with nondysplastic intestinal metaplasia.

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Overall the patients on average underwent 1.4 ablation sessions and no adverse events were recorded.

The results showed that 46% of the patients achieved complete eradication of BE, at an average endoscopic surface regression of 84%, from an average length

of 6.0 cm to 1.2 cm. It was also reported that that 71% of the seven participants with dysplasia at baseline achieved complete elimination of their dysplasia.

The researchers concluded, “We submit that it is possible, using the HALO360 system combined with its focal counterpart, HALO90, to eradicate all BE in every patient in a very safe manner, and that this intervention is considerably operator-independent. Further study will be needed to address the durability of effect and its cost-effectiveness.”

And noted, “The results from this single-operator, referral center community practice suggest that the procedure deserves attention and implementation in general clinical practice.”

Source: Roorda AK, Marcus SN, Triadafilopoulos G: Early experience with radiofrequency energy ablation therapy for Barrett’s esophagus with and without dysplasia. *Diseases Esophagus* 20(6), 516–522 (2007).