CME Answers for the month of AUGUST 2013

CONTINUING MEDICAL EDUCATION

Asthma Control Optimising Asthma Treatment in Adults. Part 1

The aim of the management of patients with asthma is to optimise their asthma control.

IN THE MEDICINE

Secondary Prevention after Ischemic Stroke or Transient Ischemic Attack

A 62-year-old woman is seen 1 week after an ischemic stroke. She had presented to another hospital with dysphasia and right-sided weakness.

JOURNAL DIGESTS

FROM REUTERS HEALTH

Unnecessary repeat cholesterol tests common: study
Treat sinusitis in kids less aggressively, says AAP guideline
Room temperature, humidity not a factor in LASIK outcomes
Antibiotics in infancy linked to eczema ...and more

CME Answers for the month of AUGUST 2013

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1. CAPRIE steering committee, Lancet 1996
2. CURE trial, Yusuf S et al, NEJM, 2001
3. CLARITY trial, Gibson C et al., Am J Cardiol, 2006

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**CME - Continuing Medical Education**
Asthma Control Optimising Asthma Treatment in Adults. Part 2

The optimal use of medications to achieve asthma control and the importance of regular monitoring and dose adjustment to lessen future risk of exacerbations, accelerated decline in lung function and medication side effects are discussed in the second part of this two-part article.

**In the Medicine**
Aspirin for Preventing the Recurrence of Venous Thromboembolism

About 20% of patients with unprovoked venous thromboembolism have a recurrence within 2 years after the withdrawal of oral anticoagulant therapy. Extending anticoagulation prevents recurrences but is associated with increased bleeding. The benefit of aspirin for the prevention of recurrent venous thromboembolism is unknown.

Notes: The above articles are subject to change without prior notice.
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**CONTINUING MEDICAL EDUCATION**

Asthma Control Optimising Asthma Treatment in Adults. Part 1
The aim of the management of patients with asthma is to optimise their asthma control. The assessment of patients’ asthma symptoms and their lung function and addressing comorbidities (such as rhinosinusitis, sleep apnoea and obesity) and risk factors (such as allergen exposure and exercise) are discussed in the first part of this two-part article.

**IN THE MEDICINE**

Secondary Prevention after Ischemic Stroke or Transient Ischemic Attack
A 62-year-old woman is seen 1 week after an ischemic stroke. She had presented to another hospital with dysphasia and right-sided weakness; magnetic resonance imaging (MRI) showed a recent infarction in the left parietal cortex, and computed tomographic angiography (CTA) showed a high-grade stenosis in the left proximal internal carotid artery with normal intracranial vessels.

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Unnecessary repeat cholesterol tests common: study

Scientists create human liver from stem cells

All types of urinary incontinence more common after vaginal delivery

Treat sinusitis in kids less aggressively, says AAP guideline

Room temperature, humidity not a factor in LASIK outcomes

Adalimumab no better than placebo for interstitial cystitis/bladder pain syndrome

Antibiotics in infancy linked to eczema

Stem-cell therapy wipes out HIV in two patients

Menthol candy makes bowel cleansing solution more palatable

Red meat tied to worse colon cancer outcomes: study

Chronic pulmonary aspergillosis responds to long-term therapy
UNNECESSARY REPEAT CHOLESTEROL TESTS COMMON: STUDY

NEW YORK (Reuters Health) - A third of cardiac patients have cholesterol monitoring more often than guidelines recommend, a new study from the Veterans Administration (VA) suggests.

The findings are “very unsurprising,” according to Dr. Michael Johansen of The Ohio State University in Columbus, who has studied cholesterol management. He said doctors may order more tests to meet (or exceed) performance measures, and because they get paid for running a cholesterol panel.

Performance measures from the American Heart Association and other groups call for annual cholesterol tests for adults with heart disease, although new guidelines are in development.

For their study, Dr. Salim Virani of the Michael E. DeBakey Veterans Affairs Medical Center in Houston tracked over 35,000 people with heart disease. All of them had their LDL cholesterol under control and hadn't recently started on any new cholesterol drugs.

Over the 11 months after patients’ most recent cholesterol test, one in three underwent a repeat test. Very few of those patients - about 6% - had any changes made to their treatment regimen as a result of the second test.

“I think a lot of it is because of the habit of (ordering) labs on patients... without really thinking about, ‘What am I going to do with this information with someone who is at target for cholesterol?’” Dr. Virani said.

People with additional health problems, such as diabetes or high blood pressure, were most likely to get their cholesterol panel repeated.

“The guidelines say so, so people do it, but there's not really anything you're going to do with those numbers,” Dr. Johansen, who wasn't involved in the new research, told Reuters Health.

Most of the study patients were already taking a cholesterol-lowering statin, he noted.

Rather than focusing on annual cholesterol testing, Dr. Johansen said, putting patients with heart disease on a statin and making sure they’re taking it might be a better use of time.

*By Genevra Pittman*

1. NAME OF THE MEDICINAL PRODUCT. PENTAXIM™ powder and suspension for suspension in prefilled syringes, diphtheria, tetanus, pertussis (acellular component); poliol (oral) type b conjugate vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION. After reconstitution one dose (0.5 ml) contains: Diphtheria toxoid 30 IU • Tetanus toxoid 150 IU. Acellular pertussis antigens: Tetanus toxoid 60 μg • Haemophilus influenzae type b 25 μg • Type 1 pneumococcal vaccine (formaldehyde-inactivated) 0.3 μg • Type 2 pneumococcal vaccine (formaldehyde-inactivated) 0.1 μg • Type 3 pneumococcal vaccine (formaldehyde-inactivated) 0.2 μg • Poliovirus of haemagglutinin type 1 25 μg • type 2 poliovirus (inactivated) 40 DU*† • type 3 poliovirus (inactivated) 32 DU*†. For excipients, see section 6.1.

3. PHARMACEUTICAL FORM. Powder in vial (type I glass) with a stopper (chlorobutyl) + 0.5 ml of suspension in prefilled syringe (glass) with a plunger stopper (chlorobutyl) + 0.5 ml of solution in prefilled syringe consisting of: Diphtheria toxoid (adsorbed on aluminium hydroxide 0.3 mg) • Diphtheria toxoid (adsorbed on aluminium hydroxide 0.3 mg). For reconstitution, see section 5.6.3. The suspension in the prefilled syringes is a mono-emulsion system (O/W) with an emulsion droplet size of 0.5 μm. The vacine must be used immediately after reconstitution.

4. CLINICAL PARTICULARS. 4.1 Therapeutic indications. This vaccine is indicated in the prevention of diphtheria, tetanus, pertussis, poliomyelitis and invasive infections caused by Haemophilus influenzae type b such as meningitis, epiglottitis, cellulitis, arthritis, epiglottitis, etc., by primary vaccination in infants from the age of 2 months for tetanus, diphtheria and poliomyelitis vaccination; one year after primary vaccination during the second year of life. This vaccine does not protect against infections caused by other types of Haemophilus influenzae nor against meningococcal disease due to other serogroups. 4.2 Pharmacology and method of administration. Penta- tox. Primary vaccination. One injection given at an interval of 4 weeks between the ages of 2 months and 18 months for tetanus, diphtheria and poliomyelitis vaccination and every 2-5 years thereafter. Inactivated polio vaccine is not given more than 6 months after the fifth dose of a live-attenuated polio vaccine. It is recommended not to administer the inactivated polio vaccine too soon after the last dose of the live-attenuated polio vaccine because of a possible interference of the immune response. Inactivated polio vaccine is not administered later than the age of 15 years. Haemophilus influenzae type b conjugate vaccine should be administered in two separate injection sites and on two different days.

4.3 Gastro-intestinal disorders. • Nervousness, irritability. • Insomnia, sleep disturbances. Uncommon reactions: • Abnormal crying, prolonged inconsolable crying.

4.4 Effects on ability to drive and use machines. 4.5 Interactions with other medicinal products and other forms of interaction. 4.6 Pregnancy and lactation. Not applicable. 4.7 Effects on ability to drive and use machines. Not applicable. 4.8 Undesirable effects. The adverse events are ranked under headings of frequency using the following convention: • Very common: ≥ 10% • Common: ≥ 1% and < 10% • Rare: ≥ 0.1% and < 1% • Very rare: ≤ 0.1% • Not applicable.

5. PHARMACEUTICAL PARTICULARS. 5.1 Local reactions. After reconstitution one dose (0.5 ml) contains: Diphtheria toxoid 30 IU • Tetanus toxoid 150 IU. Acellular pertussis antigens: Tetanus toxoid 60 μg • Haemophilus influenzae type b 25 μg • Type 1 pneumococcal vaccine (formaldehyde-inactivated) 0.3 μg • Type 2 pneumococcal vaccine (formaldehyde-inactivated) 0.1 μg • Type 3 pneumococcal vaccine (formaldehyde-inactivated) 0.2 μg • Poliovirus of haemagglutinin type 1 25 μg • type 2 poliovirus (inactivated) 40 DU*† • type 3 poliovirus (inactivated) 32 DU*†. For excipients, see section 6.1.

6. PHARMACEUTICAL PARTICULARS. 6.1 Preclinical safety data. 6.2 Pharmacological properties. Not applicable. 6.3 Precautionary information. 6.4 Special precautions for storage. Store in a refrigerator (2°C - 8°C). Do not freeze. 6.5 Nature and contents of container. Powder in vial type: glass with a stopper (chlorobutyl) + 0.5 ml of solution in prefilled syringe (glass): with a plunger stopper (chlorobutyl) + 0.5 ml of suspension in prefilled syringe (glass) with a plunger stopper (chlorobutyl). Powder in syringe type: glass with a stopper (chlorobutyl) + 0.5 ml of suspension in prefilled syringe (glass) with a plunger stopper (chlorobutyl) + 0.5 ml of solution in prefilled syringe (glass) with a plunger stopper (chlorobutyl).

LONDON (Reuters) - Scientists have for the first time made a functional human liver from stem cells derived from skin and blood and say their success points to a future when much-needed livers and other transplant organs could be made in a laboratory.

While it may take another 10 years before lab-grown livers could be used to treat patients, the Japanese scientists say they now have important proof of concept that paves the way for more ambitious organ-growing experiments.

“The promise of an off-the-shelf liver seems much closer than one could hope even a year ago,” said Dusko Illic, a stem cell expert at King’s College London who was not directly involved in the research but praised its success.

He said however that while the technique looks “very promising” and represents a huge step forward, “there is much unknown and it will take years before it could be applied in regenerative medicine.”

Researchers around the world have been studying stem cells from various sources for more than a decade, hoping to capitalize on their ability to transform into a wide variety of other kinds of cell to treat a range of health conditions.

There are two main forms of natural stem cells - embryonic stem cells, which are harvested from embryos and can give rise to any type of cell in the body, and adult stem cells, which are the progenitors of new cells needed for repairs in specific tissue families, such as muscle and bone.

The induced pluripotent stem cells (iPS cells) used in the new study are a third kind. They are created from normal tissue (often skin or blood) whose cells have been coaxed backward to a near-embryonic state.

Countries across the world have a critical shortage of donor organs for treating patients with liver, kidney, heart and other organ failure. Scientists are keenly aware of the need to find other ways of obtaining organs for transplant.

The Japanese team, based at the Okohama City University Graduate School of Medicine in Japan, used iPS cells to make three different cell types that would normally combine in the natural formation of a human liver in a developing embryo - hepatic endoderm cells, mesenchymal stem cells and endothelial cells - and mixed them to see if they would grow together.

They found the cells did grow and began to form three-dimensional “liver buds” - a collection of liver cells with the potential to develop into a full organ.

When they transplanted human liver buds into mice, the researchers found the buds matured, the human blood vessels connected to the mouse host’s blood vessels and they began to perform many of the functions of mature human liver cells.

“To our knowledge, this is the first report demonstrating the generation of a functional human organ from pluripotent stem cells,” the researchers wrote in the journal Nature.
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Malcolm Allison, a stem cell expert at Queen Mary University of London, who was not involved in the research, said the study’s results offered “the distinct possibility of being able to create mini livers from the skin cells of a patient dying of liver failure” and transplant them to boost the failing organ.

Takanori Takebe, who led the study, told a teleconference he was so encouraged by the success of this work that he plans similar research on other organs such as the pancreas and lungs.

A team of American researchers said in April they had created a rat kidney in a lab that was able to function like a natural one, but their method used a “scaffold” structure from a kidney to build a new organ.

And in May last year, British researchers said they had turned skin cells into beating heart tissue that might someday serve as a patch to treat heart failure.

That livers and other organs may one day be made from iPS cells is an “exciting” prospect, said Matthew Smalley of Cardiff University’s European Cancer Stem Cell Research Institute.

“(This) study holds out real promise for a viable alternative approach to human organ transplants,” he said.

Other experts emphasized the current importance of iPS cells in research to discover and test medicines to treat diseases.

Chris Mason, a regenerative medicine expert at University College London said the greatest impact of iPS-cell liver buds might be in their use to improve drug development.

“Presently to study the metabolism and toxicology of potential new drugs, human cadaveric liver cells are used,” he said. “Unfortunately these are only available in very limited quantities”.

The suggestion from this new study is that mice transplanted with human iPS-cell liver buds might be used to test new drugs to see how the human liver would cope with them and whether they might have side-effects such as liver toxicity.

By Kate Kelland

ALL TYPES OF URINARY INCONTINENCE MORE COMMON AFTER VAGINAL DELIVERY

NEW YORK (Reuters Health) - Women who give birth vaginally have a higher rate of all types of urinary incontinence compared with those who get Cesarean sections, Swedish researchers have found.

“It has earlier been reported that stress urinary incontinence is the only subtype linked to vaginal delivery and that urge urinary incontinence might be associated with caesarean section,” Dr. Maria Gyhagen from Sahlgrenska Academy at Gothenburg University told Reuters Health by email.

“To us it was most surprising that vaginal delivery was associated -- and approximately to the same extent (50% odds increase) -- with an increased risk of all three subtypes of urinary incontinence,” she said.
Dr. Gyhagen and colleagues used data from the SWEdish Pregnancy, Obesity, and Pelvic floor (SWEPOP) study to understand the relationships between mode of delivery and prevalence, severity, and bothersomeness of stress urinary incontinence (SUI), urge urinary incontinence (UUI), and mixed urinary incontinence (MUI) 20 years after one birth.

Of the 5,118 women included in the study, published online June 21 in BJOG, 15.3% had SUI, 6.1% had UUI, and 14.4% had MUI.

Compared with women who had had C-sections, women who had delivered vaginally had 42% greater odds of SUI, 66% greater odds of UUI, and 46% greater odds of MUI after adjustment for maternal age, body mass index and infant birth weight (all differences significant).

Among incontinent women, moderate to severe symptoms of SUI and UUI were slightly more common among women with vaginal delivery, whereas similar proportions of the two groups had moderate to severe MUI.

Bothersome urinary incontinence was significantly more prevalent after vaginal delivery (11.2%) than after C-section (6.3%).

There was no significant difference between the two groups in bothersomeness of SUI and UUI, but bothersomeness of MUI was significantly more common after vaginal delivery (40.0% vs. 29.9%).

The prevalence of significant urinary incontinence was also significantly higher after vaginal delivery (9.7% vs. 5.7%).

Only a minority of incontinent women (251/1,899, 13.2%) had consulted a doctor, although the prevalence was significantly higher after vaginal delivery than after C-section (5.2% vs. 3.7%); treatment for urinary incontinence was even less prevalent.

Symptomatic pelvic organ prolapse contributed significantly to the prevalence, duration, type, and degree of bother of urinary incontinence.

“It should be noted that a causal link between vaginal birth/trauma and urinary incontinence cannot be shown by a statistical association alone and must be supported by pathophysiological knowledge from other fields of investigation,” the researchers note. “There are, however, studies using magnetic resonance imaging, ultrasound and neurophysiological techniques that have been published supporting a causal relationship between vaginal delivery and pelvic floor damage.”

They add that “it is important to inform women about the predictable, preventable, and reversible effect on urinary continence of overweight and obesity, a precaution and measure that may be most urgent after vaginal delivery.”

Dr. Gyhagen echoed this sentiment. The most important intervention to prevent urinary incontinence after vaginal delivery, she said, is “to obtain and preserve a normal weight.”

*By Will Boggs, MD*  
*BJOG 2013.*
TREAT SINUSITIS IN KIDS LESS AGGRESSIVELY, SAYS AAP GUIDELINE

NEW YORK (Reuters Health) - Children with persistent sinusitis may be treated with antibiotics or observed for a few days to see if they get better on their own, according to updated guidelines from the American Academy of Pediatrics (AAP).

“Most children with a runny nose do not need antibiotics,” lead author Dr. Ellen R. Wald told Reuters Health by email. “These new guidelines will help pediatricians accurately diagnose which children have a common cold -- which antibiotics won't help -- and which children have a bacterial infection that will get better with antibiotics.”

In a statement aimed at parents, Dr. Wald, chair of the AAP Subcommittee on Acute Sinusitis, said “Children with persistent sinusitis may be managed with either an antibiotic or with an additional brief period of observation, allowing the child up to another 3 days to fight the infection and improve on his or her own.”

“The choice to treat or observe,” she added, “should be discussed with your doctor and may be based on your child’s quality of life and how much of a problem the sinusitis is causing. In contrast, all children diagnosed with severe or worsening sinusitis should start antibiotic treatment to help them recover faster and more often.”

Dr. Wald also said that although antibiotic treatment may be expected, it may not be appropriate.

“Some episodes of persistent sinusitis include relatively mild symptoms that may improve on their own in a few days. In addition, antibiotics can have adverse effects, which may include vomiting, diarrhea, upset stomach, skin rash, allergic reactions, yeast infections, and development of resistant bacteria (that make future infections more difficult to treat).”

The guidelines were published online on June 24 in Pediatrics. They discourage clinicians from obtaining “imaging studies of any kind to distinguish acute bacterial sinusitis from viral URI (upper respiratory infection), because they do not contribute to the diagnosis.”

Amoxicillin with or without clavulanate is recommended as first-line treatment of acute bacterial sinusitis. “Clinicians should reassess initial management if there is either a caregiver report of worsening (...) or failure to improve within 72 hours of initial management,” the guidelines say.

Nevertheless, the authors note that evidence is scant. Since 2001, when the previous guideline was released, “Ironically, the number of published guidelines on the topic (5) exceeds the number of prospective placebo-controlled clinical trials of either antibiotics or ancillary treatments of acute bacterial sinusitis.”

According to Dr. Michael J. Smith, author of a technical report accompanying the guidelines, “There are only a few high-quality randomized controlled studies focusing on the treatment of acute bacterial sinusitis in children. Two showed that antibiotics helped treat sinusitis and the others did not. This was in large part due to different characteristics -- such as severity of illness -- between the children enrolled in each study.”

“Examining these differences, allowed our guideline committee to make an evidence-based recommendation about which children warrant treatment...”
for sinusitis,” Dr. Smith, of the University of Louisville School of Medicine in Kentucky, told Reuters Health by email.

The technical report also points out that the efficacy of decongestants and antihistamines for sinusitis has not been proven. “Given recent concerns regarding their safety profile in young children, the use of these agents should be avoided,” the report says.

By David Douglas

Pediatrics 2013.

ROOM TEMPERATURE, HUMIDITY NOT A FACTOR IN LASIK OUTCOMES

NEW YORK (Reuters Health) - During LASIK, procedure room temperature and humidity don’t have any meaningful effect on the refractive outcome, according to a large retrospective cohort study.

A few reports from smaller patient populations have suggested that ambient temperature or humidity in the LASIK room may have a clinically significant effect on refractive outcome, the study team notes in a report online June 14 in Ophthalmology.

“Many surgeons believe that their surgical outcomes are directly related to the temperature and/or the humidity in their refractive procedure rooms,” first author Dr. Michael Seider from the University of California, San Francisco told Reuters Health.

“Indeed, many surgeons have expensive and elaborate climate-control systems in their refractive suites and may refuse to operate if the environmental parameters are considered outside of some acceptable range,” he said.

But in looking at data on more than 200,000 eyes treated by LASIK at an Optical Express, Inc, location in the UK and Ireland, Dr. Seider and colleagues found that neither room temperature nor humidity during LASIK had any clinically significant effect on outcome.

When considering all eyes, an increase of 1 degree Celsius during LASIK was associated with a 0.003 diopter more hyperopic refraction one month postoperatively, and an increase of 1% in humidity was associated with a 0.0004 more myopic refraction, they report.

“These findings also were robust despite flap technique or location of surgery and within individual subgroups on the basis of age, refractive error, and gender,” they say.

“I believe our data are the most convincing available regarding this issue - particularly because of the vast number of patients,” Dr. Seider told Reuters Health. The study sample includes approximately 500 times more eyes than those in the previous reports.

The investigators say the VISX Star S4 IR excimer laser was used for all eyes in their series. The manufacturer recommends it be operated with an ambient temperature between 15 degrees C and 27 degrees C (60 to 80 degrees Fahrenheit) and with 35% to 65% relative humidity.

In their population, no eyes were treated at ambient temperatures of 15 degrees C or less, although 414 eyes were treated at 27 degrees C or more. In addition,
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42,657 eyes were treated at 35% or less relative humidity, and 320 eyes were treated with 65% or more relative humidity.

The authors say they independently evaluated the groups of eyes that were treated outside the manufacturer’s recommendations and found no clinically significant effect of temperature or humidity on postoperative refractive error in those groups.

One author on the study has disclosed a relationship with Optical Express, Inc. The other authors have no disclosures.

By Megan Brooks
Ophthalmology 2013.

ADALIMUMAB NO BETTER THAN PLACEBO FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

NEW YORK (Reuters Health) - While adalimumab improves virtually all measures of interstitial cystitis/bladder pain syndrome (IC/BPS), it failed to outperform placebo in a new pilot trial.

Adalimumab blocks the effects of TNF-alpha, and drugs that inhibit TNF-alpha have decreased bladder inflammation in experimental models of IC/BPS.

Dr. Philip C. Bosch, from Palomar Medical Center in Escondido, California, conducted the new proof-of-concept study after an IC/BPS patient had seen his symptoms resolve with adalimumab treatment for Crohn's disease.

Of 43 patients with IC/BPS, 21 were randomized to adalimumab and received an 80-mg subcutaneous loading dose followed by 40 mg subcutaneously every two weeks for 12 weeks. The other 22 patients got placebo injections on the same schedule, according to the report, online June 21 in The Journal of Urology.

The study was terminated early after half of the 43 patients demonstrated a dramatic and statistically significant clinical improvement.

Patients randomized to adalimumab experienced statistically significant improvements in all outcome measures, including the O’Leary-Sant Interstitial Cystitis Symptom and Problem Indexes (overall score and individual indices) and the Pelvic Pain, Urgency, Frequency scale.

More than half the patients in the adalimumab group (53%) were moderately or greatly improved or asymptomatic at week 12.

However, because of similar improvements in the placebo group, including a 50% responder rate, there was no statistically significant improvement in any of the adalimumab group outcome measures from baseline to week 2, 6, or 12.

Apart from transient local injection site reactions in four adalimumab patients, there were no significant adverse events.

“Adalimumab failed to demonstrate positive proof of concept compared to placebo due to a significant placebo effect,” Dr. Bosch writes in his report. “The significant placebo effect seen with just advice and support in treatment studies of IC/BPS should be further examined.”

Dr. Jochen Neuhaus from University of Leipzig in Germany, who recently reviewed treatment options for IC/BPS (Nat. Rev. Urol. 2012;9:707-720), was not surprised at these results.
“Autoimmune diseases have been seen in conjunction with IC, but so far there is no proof for a direct causal relationship,” he told Reuters Health by email. “Thus, containing immune reaction and local inflammation can be helpful, but is only the first step in a cascade of events necessary to restore bladder structure (urothelial barrier) and function.”

“Treatment has to be focused on restoration of bladder structure,” Dr. Neuhaus added. “Instillation therapies with chondroitin sulfate (plus hyaluronic acid) have shown the most promising for GAG-layer repair. Functional improvements can be achieved by modulation of receptor expression via BoNT-A (botulinum toxin serotype A) intravesical injections.”

“Unfortunately, adalimumab did not prove to have a significant effect on IC symptoms compared to placebo,” he concluded. “Therefore, it cannot be recommended as therapy option.”

Dr. Chris Elliott, who also wasn’t involved in the new study, said IC/BPS is poorly understood.

“To date we are without a gold-standard test to diagnose the condition,” Dr. Elliott, from Stanford University’s Department of Urology, told Reuters Health by email. “Moreover, the cause(s) of patient symptoms (immunologic, musculoskeletal or neural) are unclear. Successful treatment has been shown with neuromodulation, myofascial release, immunosuppression, and other pharmacologic therapies. I think the variety of treatments that are currently being used only underscores the complexity of the problem.”

“As evidenced in this small trial,” Dr. Elliott said, “placebo-controlled studies are a must for IC/BPS research given the high placebo response rates which can be seen (and were higher than normal in this small study). The author should be commended for studying the effects of adalimumab on patients with IC/BPS in the proper fashion. Despite a negative result, the study teaches us a lot.”

Dr. Bosch could not be reached for comments.

_by Will Bogg, MD
J Urol 2013._
ANTIBIOTICS IN INFANCY LINKED TO ECZEMA

NEW YORK (Reuters Health) - In a new review of previous research, children who took antibiotics in their first year of life were about 40% more likely to develop eczema.

Exposure to antibiotics in utero was not tied to eczema, however, according to the results published June 20th online in the British Journal of Dermatology.

Experts said the new study supports the idea that antibiotics destroy intestinal microbes that play an important role in the immune system's development after birth.

The study brings us closer to understanding the possible link between antibiotics and eczema, Dr. Ruchi Gupta, of Northwestern School of Medicine in Chicago, told Reuters Health by email.

“They may be linked through the hygiene hypothesis,” said Dr. Gupta, who was not involved in the new study. Disturbing one element of the delicate developing immune system could result in allergic skin reactions like eczema, she said.

Previous research had suggested that early life exposure to antibiotics may lead to an increased risk for eczema, but the new review is the first to consolidate available results from several studies.

Researchers led by Dr. Teresa Tsakok of Guy’s and St Thomas’ Hospital NHS Foundation Trust in London, UK, evaluated the results of 20 studies of antibiotic use, either prenatally or in the first year of life, in connection with later skin problems.

They found no link between prenatal antibiotic exposure and eczema, but exposure to the drugs in the first year of life increased the risk for the disease by up to 40%.

The more antibiotics a baby took, the higher the risk. With each additional round of antibiotics, eczema risk rose by 7%. Broad-spectrum antibiotics appeared to have the strongest effect.

Dr. Gupta said the researchers may have overlooked some cases of “reverse causation,” in which infants with eczema have more skin infections that may require antibiotics and confound the results, but the authors acknowledged that limitation and say the findings are still valid.

Dr. Tsakok and her coauthors did not respond by press time to a request for comments.

“The study clearly supports the theory that antibiotics in infancy increase the risk of eczema,” said Dr. Thomas Abrahamsson, a pediatrician who studies skin disorders at Linköping University in Sweden.

But, he told Reuters Health, there was another weakness in the review: some studies lacked precise information about when eczema symptoms began and when antibiotics were first administered.

“The conclusion of the article, however, is sound,” Dr. Abrahamsson said. “Antibiotics should only be used when it is really necessary.”

By Kathryn Doyle
STEM-CELL THERAPY WIPES OUT HIV IN TWO PATIENTS

LONDON (Reuters) - Two men with HIV have been off AIDS drugs for several months after receiving stem-cell transplants for cancer that appear to have cleared the virus from their bodies, researchers reported on Wednesday.

Both patients, who were treated in Boston and had been on long-term drug therapy to control their HIV, received stem-cell transplants after developing lymphoma, a type of blood cancer.

Since the transplants, doctors have been unable to find any evidence of HIV infection, Timothy Henrich of Harvard Medical School and Brigham and Women's Hospital in Boston told an International AIDS Society conference in Kuala Lumpur.

While it is too early to say for sure that the virus has disappeared from their bodies altogether, one patient has now been off antiretroviral drug treatment for 15 weeks and the other for seven weeks.

Last July Dr. Henrich first reported that the two men had undetectable levels of HIV in their blood after their stem-cell treatment, but at that time they were still taking medicines to suppress HIV.

Using stem-cell therapy is not seen as a viable option for widespread use, since it is extremely expensive, but the latest cases could open new avenues for fighting the disease, which infects about 34 million people worldwide.

The latest cases resemble that of Timothy Ray Brown, known as “the Berlin patient,” who became the first person to be cured of HIV after receiving a bone marrow transplant for leukemia in 2007. There are, however, important differences.

While Brown’s doctor used stem cells from a donor with a rare genetic mutation, known as CCR5 delta 32, which renders people virtually resistant to HIV, the two Boston patients received cells without this mutation.

“Dr. Henrich is charting new territory in HIV eradication research,” Kevin Robert Frost, chief executive officer of the Foundation for AIDS Research, which funded the study, said in a statement.

The latest antiretroviral AIDS drugs can control HIV for decades. But many people still do not get therapy early enough, prompting the World Health Organization to call for faster roll-out of medicines after patients test positive.

By Ben Hirschler

MENTHOL CANDY MAKES BOWEL CLEANSING SOLUTION MORE PALATABLE

NEW YORK (Reuters Health) - Sugar-free menthol candy makes it easier to consume polyethylene glycol electrolyte solution (PEG-E) before colonoscopy, Lebanese researchers say.

Candy consumption “is a cheap, safe, simple, and effective method to improve palatability of the solution, (and) enhance adherence and compliance, which translates into improved bowel preparation,” Dr. Ali I. Sharara told Reuters Health by email.
In a June 12 online paper in Gastrointestinal Endoscopy, Dr. Sharara and colleagues at the American University of Beirut Medical Center say a few patients had mentioned to them that sucking menthol candy drops (often used as a cough suppressant) improved the taste and tolerability of the solution.

To investigate further, the team randomized 99 patients to split-dose 4-L PEG-E with or without candy drops. Patients in the candy group received a packet containing 15 sugar-free colorless menthol candy drops (Halls) and were told to suck on the drops while drinking the liquid. Each drop contained 5.2 mg of menthol. Patients were asked to rate the palatability of the experience on a scale ranging from 1 (disgusting) to 5 (tasty).

Mean palatability scores were significantly higher in the candy group (3.9) than in controls (2.8). In addition, the proportion of patients deemed to have excellent preparation was much higher in the candy group (63.3% vs 34.0%). Side effects were similar, except the rate of nausea was significantly lower in the candy group (24.5% vs 44.0%).

On multivariate analysis, excellent preparation was associated with candy drops (odds ratio, 3.3) and with a smaller unconsumed volume of same-day PEG-E.

The researchers say the approach has no disadvantages and results in “improved tolerability and an improved bowel cleansing effect, with a high rate of excellent grade preparations with minimal dietary and patient burden.”

By David Douglas
Gastrointest Endosc 2013.

RED MEAT TIED TO WORSE COLON CANCER OUTCOMES: STUDY

NEW YORK (Reuters Health) - People who report eating the most red and processed meat before being diagnosed with colon cancer are more likely to die during the next eight years, according to a new study.

“It’s another important reason to follow the guidelines to limit the intake of red and processed meat,” said Dr. Marjorie McCullough, the study’s lead author from the American Cancer Society in Atlanta.

While the new study can’t prove eating red or processed meats causes colon cancer deaths, previous studies have tied these meats to an increased risk of colon cancer. There’s less evidence, however, on how people’s diets after colon cancer diagnoses affect their chances of survival.

For the new research, Dr. McCullough and her colleagues used data on 2,315 men and women who were diagnosed with colon or rectal cancer between 1992 and 2009. Overall, 966 of them died between the start of the study and December 31, 2010. The researchers found no link between how much red or processed meat a person ate after their diagnosis and their risk of death, but the amount of meat a person ate before their diagnosis was tied with their risk of dying during the study.

About 43% of the 580 people who ate about 10 servings of red or processed meat per week at the start of the study died during follow up, compared to about 37% of the 576 people who ate about two servings per week.
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The researchers also found that people who consistently ate more red or processed meat before and after their colon cancer diagnosis were more likely to die from that cancer during the study, compared to those who at the least before and after diagnosis.

Dr. Jeffrey Meyerhardt, who wrote an editorial accompanying the new study in the Journal of Clinical Oncology, said it's possible that the link between red and processed meats and colon cancer comes from cancer-causing compounds found in cooked meat or preservatives.

“The primary message is a confirmation that increased intake of red or processed meat can have detrimental effects on the development of colon cancer, the type of cancer and other health effects of patients in the long term,” said Dr. Meyerhardt, of the Dana-Farber Cancer Institute in Boston.

Dr. McCullough said about three or four servings of red or processed meats per week is a good target for people.

“We're not saying people need to be vegetarians. It's really just limiting intake and making it more the exception than the rule,” she said.

By Andrew M. Seaman
J Clin Oncol 2013.

CHRONIC PULMONARY ASPERGILLOSIS Responds to Long-Term Therapy

NEW YORK (Reuters Health) - Health status in patients with chronic pulmonary aspergillosis improves with long-term antifungal treatment, UK researchers report.

“Our contribution is to add a direct validated means of assessing progress, and noting that 15-20% of patients do really well, with major (improvement), about 60% stabilize and are better, and the remainder do poorly, requiring IV therapy and possibly gamma IFN therapy,” Dr. David W. Denning told Reuters Health.

“The key message from our paper is that those treated long term (who can tolerate one or more of the drugs) do much better,” he added in an email.

But the management issues are complex, Dr. Denning said.

Drug interactions are often a problem, drug doses frequently need to be modified because metabolism can vary (for example, 20% of northeast Asians are slow voriconazole metabolizers), multiple parameters must be monitored to assess response and detect failure on therapy, andazole drug resistance can emerge during therapy, Dr. Denning pointed out.

He added, "Physicians experienced with antifungal therapy are best placed to manage these patients."

Left untreated, more than 50% of patients with chronic pulmonary aspergillosis die within five years. Until now, no study used validated tools to examine the effect of antifungal therapy on patients' health status.

In their study of 122 patients, Dr. Denning from the UK’s National Aspergillosis Center at The University of Manchester and colleagues administered the St. George’s respiratory questionnaire (SGRQ) every three months for a year to evaluate the effect of long-term antifungal treatment in improving or stabilizing their health status.
The SGRQ score ranges from 1 to 100, with higher scores indicating worse health status. Changes of at least 4 points are considered clinically significant, the authors explained online June 20th in Clinical Infectious Diseases.

Clinically significant improvements were seen in 47.4% of patients at six months and 49.5% at 12 months, whereas 31.5% at six months and 31.8% at 12 months reported deterioration. The rest of the patients remained stable at six (21.1%) and 12 (18.7%) months.

About two-thirds of patients who stayed on the same antifungal treatment for three to six months either improved or remained stable. Extending treatment from three to six months increased the rate of improvement and reduced the rate of deterioration.

Among 44 patients who remained on the same antifungal agent for 12 months, 23 (52%) improved, nine (20%) remained stable, and 12 (30%) deteriorated. Most patients who deteriorated were on itraconazole, and side effects may have contributed to their deterioration in health status, the authors suggest.

The 44 patients who remained on the same agent for 12 months had better health status than the 28 patients who changed to different agents and the 35 patients who had intermittent periods with no treatment, but the differences were not statistically significant.

Overall, 46 patients reported at least one side effect. Patients with side effects had significantly worse health status at 12 months than those who did not have side effects.

One of the factors associated with better responses appeared to be the drug used, the researchers note, with posaconazole providing slightly better results than voriconazole, which in turn was better than itraconazole.

“More therapeutic approaches for this infectious progressive disease are urgently needed,” the investigators say.

“One cavititation or upper lobe fibrosis patient should be tested for chronic pulmonary aspergillosis with an Aspergillus antibody test (not antigen), and worked up,” Dr. Denning added. “Making the diagnosis is critical, and is often delayed for years.”

By Will Boggs, MD
Asthma Control Optimising Asthma Treatment in Adults. Part 1

The aim of the management of patients with asthma is to optimise their asthma control.

IN THE MEDICINE
Secondary Prevention after Ischemic Stroke or Transient Ischemic Attack
A 62-year-old woman is seen 1 week after an ischemic stroke. She had presented to another hospital with dysphasia and right-sided weakness.

JOURNAL DIGESTS FROM REUTERS HEALTH
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1. Patients suffering from MI, Ischemic Stroke or established PAD
2. Patients suffering from Acute Coronary Syndrome:
   - NSTEMI including patients undergoing a stent placement following PCI, in combination with ASA
3. STEMI in combination with ASA in medically treated patients eligible for thrombolytic therapy

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- Patients suffering from MI, Ischemic Stroke or established PAD
- Patients suffering from Acute Coronary Syndrome:
  - NSTEMI including patients undergoing a stent placement following PCI, in combination with ASA
- STEMI in combination with ASA in medically treated patients eligible for thrombolytic therapy

1. CAPRIE steering committee, Lancet 1996
2. CURE trial, Yusuf S et al, NEJM, 2001
3. CLARITY trial, Gibson C et al, Am J Cardiol, 2006

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