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***Helicobacter pylori* may protect children from asthma**

According to recent findings presented at the 45th Annual Meeting of the Infectious Diseases Society of America in early October 2007, the bacteria that causes stomach ulcer may, at the same time, protect children from asthma.

Helicobacter pylori has been a resident of the human stomach for thousands of years. In the USA, 30% of the adult population carries the bacterium, 50% of whom acquired *H. pylori* by age 6 years. *H. pylori* infection increases with poor living conditions, and in developing countries, 90% of the adult population may be infected. The bacterium causes chronic inflammation of the inner lining of stomach, leading to stomach ulcer and potentially stomach cancer.

Improved living condition and increased use of antibiotics have led to a decrease in *H. pylori* infection in the USA. Less than 10% of American children younger than 13 years of age now carry the bacterium, while this percentage was more than 50% 50 years ago. Meanwhile, asthma incidence in children is on the rise.

Recent findings based on the National Health and Nutrition Examination Survey involving 3327 children aged 3–13 years revealed that those carried *H. pylori* were 53% less likely to experience asthma than those who did not have the bacterium. Early-onset asthma (before 5 years of age) was also 44% less likely to happen in children who were already infected with *H. pylori*.

"It is clear that there is a biological cost to having *H. pylori* in an increased risk for getting ulcers and stomach cancer, but these typically occur relatively late in life," said Martin Blaser of New York University School of Medicine (NY, USA). "Meanwhile, asthma is a serious diagnosis especially in young children and can be deadly."

Beside asthma prevention, "*H. pylori* could be beneficial in other ways.

For instance, we found that people with the bacteria were less likely to have had recent bouts of wheezing, allergic rhinitis, dermatitis, eczema or rash," said Yu Chen, the coauthor of the study. "Other studies have shown that it may protect against gastroesophageal reflux disease and esophageal cancer."

Although more research is needed to elucidate the exact mechanisms by which *H. pylori* may prevent asthma development, the findings imply a potential *H. pylori*-based asthma treatment. "If future studies confirm and extend our findings, one concept to consider is introducing *H. pylori* or something similar into the system to provide a protective effect," said Blaser.

Source: The Infectious Diseases Society of America, VA, USA: www.idsociety.org; Chen Y, Blaser MJ. *Helicobacter pylori* colonization is inversely associated with childhood asthma. Presented at the 45th Annual Meeting of the Infectious Diseases Society of America, San Diego, CA, USA, 4–7 October 2007.

Prexige® withdrawn from Canadian market

Health Canada has stopped the sale of Prexige® (lumiracoxib), an anti-inflammatory drug, in Canada and canceled the drug's market authorization on ground of potential drug-related serious liver adverse events.

Prexige is a nonsteroidal COX-2 inhibitor. COX-2 enzyme produces prostaglandins that cause inflammation. Since November 2006, Prexige has been marketed in Canada for the treatment of osteoarthritis in adults at a maximum daily dose of 100 mg.

Following the withdrawal of Prexige in Australia in August 2007 due to two cases of serious liver adverse events linked to the drug dosage of 200 and 400 mg daily, Health Canada has requested and reviewed additional safety information from the drug's manufacturer, Novartis Pharmaceuticals Canada Inc., before coming to the decision to remove Prexige from the Canadian market.

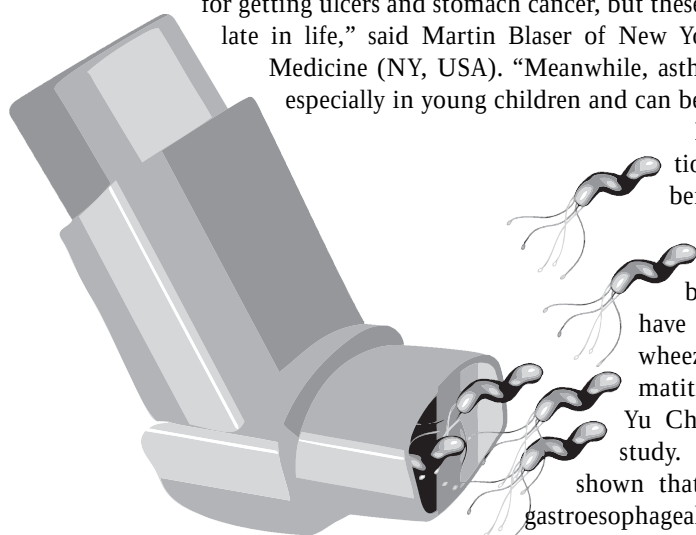
Worldwide, there have been four cases of serious liver-related adverse events associated with the use of Prexige 100 mg daily, including two cases in Canada.

Source: Health Canada: www.hc-sc.gc.ca

Novel drug for rheumatoid arthritis enters Phase I clinical trial

A novel biological agent, ARG098, for the treatment of rheumatoid arthritis (RA) has entered a Phase I clinical trial in Belgium. The study will evaluate safety, tolerability, efficacy and pharmacokinetics of the drug administered to the knee joint cavity of RA patients.

RA is a chronic autoimmune disease presenting with inflammation of the joints. The main clinical feature of RA is



the inflamed synovial membrane, which is caused by abnormal proliferation of synovial cells leading to excessive secretion of inflammatory cytokines, such as TNF- α , IL-1 and IL-6. Immune cells are recruited at the site of inflammation as a result, and surrounding tissues, including cartilage, bone and ligaments, are subsequently attacked by the immune system, causing swelling and pain.

ARG098 is a monoclonal antibody against Fas molecules on synovial cells. The binding of ARG098 and Fas will lead to apoptosis of synovial cells and subsequent reduction of synovium inflammation. Unlike currently available anti-RA drugs, such as etanercept and infliximab, which bind and neutralize TNF- α , ARG098 directly targets synovial cells.

The new drug was discovered in a collaborative study between Argenes Inc. (Japan) and Santen Pharmaceutical Co. Ltd (Japan), and Argenes now holds the license for drug development. "This is a significant progress in the long history of Fas molecule research because ARG098 is the first Fas targeting antibody that enters into a clinical study. IgM structure of ARG098 makes it possible because of more preferable characteristics for the therapeutics than IgG, which is the most common structure for existing antibody drug," said Argenes' president Masaru Kamishohara.

"Establishing the clinical study network in Europe, we will accelerate the clinical development," added Argenes' chairman Kusuki Nishioka. Argenes will start clinical trials in Japan this year.

Source: Argenes Inc., Japan: www.argenes.co.jp

Phase III study of ustekinumab for psoriasis treatment showed encouraging results

Results from the multicenter, randomized, double-blind, placebo-controlled Phase III trial evaluating the safety and efficacy of ustekinumab (CNTO 1275) in treatment of patients with moderate-to-severe plaque psoriasis (the Psoriasis Followed by Long-Term Extension [PHOENIX]-2 trial) have been presented at the 21st World Congress of Dermatology early in October 2007. Two doses of ustekinumab resulted in a 75% reduction of psoriasis as measured by Psoriasis Area and Severity Index (PASI 75) at week 12 in more than two-thirds of the 1230 patients participating in this clinical trial. A further injection of the drug at week 16 maintained the PASI 75 response through to week 28. Improvements in quality-of-life measures were seen in treated patients from week 4 of treatment compared with patients receiving placebo.

Psoriasis is a chronic, immune-mediated condition in which skin cells mature within 1 week instead of the normal rate of 4 weeks. The body cannot shed old cells as quickly as the cells mature, resulting in accumulation of dead cells as scaly plaques on affected parts of the body. The cause of psoriasis is unknown and patients usually present with high levels of IL-12 and -23 cytokines that play a role in inflammation. Approximately 125 million people are affected worldwide, including 2% of US and European populations. Almost a quarter of psoriasis patients are considered to have moderate-to-severe disease, with approximately 30% of the body surface affected.

"Psoriasis is an inflammatory disease that can cause severe emotional, physical and social burdens for patients," said

Richard Langley of Dalhousie University (NS, Canada), an investigator of the trial. "While more therapies have become available for the treatment of psoriasis over the years, dermatologists need additional options to manage this chronic disease and ustekinumab would represent a much needed addition in the treatment armamentarium."

Ustekinumab is developed by Centocor Inc. (PA, USA), for the treatment of moderate-to-severe plaque psoriasis. The drug is a fully human monoclonal antibody that targets IL-12 and -23. Throughout the study, the drug was well tolerated and percentages of adverse events were comparable between treated patients and placebo controls.

"These findings provide further evidence of the role of IL-12/23 in the pathogenesis of psoriasis and the promise that a new therapeutic approach like ustekinumab may hold for dermatologists and their patients living with this chronic, immune-related disease," said Craig Leonardi of St Louis University Medical School (MO, USA), the study's lead investigator. "The efficacy and safety data for ustekinumab in the treatment of psoriasis are exciting for the dermatology community."

"These findings show that by targeting IL-12/23 with ustekinumab, we may be able to offer dermatologists and patients a new, promising biologic therapy with an infrequent dosing regimen for the treatment of psoriasis," said Jerome Boscia, senior vice-president of clinical research and development of Centocor Inc. "We are encouraged by the results from the Phase III program and look forward to collaborating with regulatory authorities around the world in an effort to bring ustekinumab to physicians and patients in need of new therapeutic options."

Source: Centocor Inc., PA, USA: www.centocor.com; Leonardi C. Hot spot: CNTO 1275 (anti-IL-12/23p40) treatment of psoriasis: Phase III trial results. Presented at the 21st World Congress of Dermatology, Buenos Aires, Argentina, 30 September–5 October 2007.

New insights into the cause of ulcerative colitis

Ulcerative colitis is a form of inflammatory bowel disease (IBD) that involves inflammation of the lining of the rectum and large intestine. The cause of ulcerative colitis is unknown and the disease may be genetically inherited and immune related, and could involve microorganism infections. Recent findings published in the October issue of the journal *Cell* suggested that deficiency in an immunoregulatory protein, T-bet, may be the cause of this disease.

T-bet deficiency in dendritic cells leads to higher production of the cytokine TNF- α from these cells, which in turn cause inflammation and damage of the cells lining the intestinal wall. This also allows for bacterial invasion. Ulcerative colitis, together with Crohn's disease (another type of IBD

that involves not only the colon but also the small intestine), affects more than 1 million people in the USA. Approximately 20% of ulcerative colitis patients have a close relative with IBD, suggesting genetic involvement. Current treatment for IBD includes antibodies against TNF- α , which

blocks inflammation but also has side effects.

Researchers from the Harvard School of Public Health (MA, USA) have created T-bet-deficient mice that presented symptoms of

ulcerative colitis similar to that in

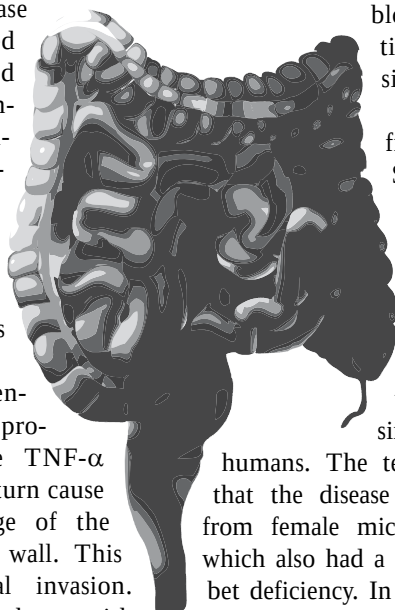
humans. The team then showed that the disease could be passed from female mice to baby mice, which also had a similar level of T-bet deficiency. In addition, the disease could also be passed among sick animals and healthy ones through physi-

cal and fecal–oral contact, suggesting the involvement of microorganisms that might have been induced by the breakdown of immune regulation.

“We have identified a new molecular player, T-bet, and when it is missing, there is spontaneous onset of the disease in the mice,” said Laurie Glimcher, the lead author of the study. “The importance of this study is that we now have a novel model for ulcerative colitis: the disease appears in 100% of the animals and looks just like the human disease.”

Interestingly, ulcerative colitis in mice could also be prevented through the use of anti-TNF- α antibodies. The researchers are looking into alternative treatments, such as increasing T-bet levels, injecting regulatory T cells to suppress inflammation, or introducing beneficial bacteria (probiotics) to compete with harmful bacteria.

Source: Harvard School of Public Health, MA, USA: www.hsph.harvard.edu; Garrett WS, Lord GM, Punit S *et al.* Communicable ulcerative colitis induced by T-bet deficiency in the innate immune system. *Cell* 131, 1–13, (2007).



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Duc Hong Le,
Commissioning Editor,
Expert Review of Clinical Immunology,
Future Drugs Ltd, Unitec House,
2 Albert Place, London N3 1QB, UK
E-mail: d.le@future-drugs.com
Tel: +44 (0)20 8349 2033;
Fax: +44 (0)20 8343 2313