



Research

PANCREATIC CANCER ACTION NETWORK

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PANCREATIC CANCER: NEWS & UPDATES

July 2010

Elevated Level of Anterior Gradient-2 in Pancreatic Juice from Patients with Pre-Malignant Pancreatic Neoplasia

<http://www.molecular-cancer.com/content/pdf/1476-4598-9-149.pdf>

Together with her colleagues, Dr. Ru Chen, a 2006 Pancreatic Cancer Action Network – AACR Career Development Award recipient, applied quantitative proteomics to identify aberrantly elevated proteins in pancreatic juice samples derived from patients with PanIN3. Twenty proteins were found elevated in all three PanIN juices by at least two-fold. Among these proteins, anterior gradient-2 (AGR2) was found to be two to ten times elevated in PanIN3 juice samples. The results suggest that elevation of AGR2 levels in pancreatic juice occurs in early pancreatic cancer progression and could be further investigated as a potential candidate juice biomarker for early detection of pancreatic cancer.

UNC Lineberger Scientists Identify Molecular Predictor of Prognosis for Pancreatic Cancer Patients

http://www.eurekalert.org/pub_releases/2010-07/uonc-uls071210.php

A new finding from scientists at UNC Lineberger Comprehensive Cancer Center may help identify patients who have more aggressive disease. The UNC team analyzed gene profiles of pancreatic tumors from patients with both localized and metastasized disease. They identified a six-gene "signature" associated with metastatic disease. This study is the first to demonstrate that molecular differences in metastatic pancreatic cancer can be identified at earlier stages and that these differences are predictive of future disease behavior. This finding, if verified in further clinical studies, could help patients and physicians make more informed decisions about treatment and could offer new research opportunities into potential therapeutic targets to treat the disease.

Johns Hopkins Medical Center Performs First Laparoscopic Pancreas Removal for Cancers

(includes 2-minute video)

<http://www.abc2news.com/dpp/news/health/johns-hopkins-medical-centers-performing-laparoscopic-pancreas-removal-for-cancers->

Johns Hopkins surgeons did their first laparoscopic Whipple operation. Generally, the Whipple operation is a six or seven-hour invasive operation where an incision is made all the way up the patient's abdomen leaving a big scar that can become infected. Hopkins surgeons, Drs. Martin Makary and Barish Edil, were able to avoid the big incision by doing parts of the Whipple operation laparoscopically – through tiny incisions.

Amplimed Phase II Study Results Show No Improvement in Overall Survival for Gemcitabine and Amplimexon in Advanced Pancreatic Cancer

<http://www.financialpost.com/news/AmpliMed+Results+Trial+Gemcitabine+Amplimexon+Advanced+Pancreatic+Cancer/3258869/story.html>

AmpliMed Corporation announced results from AMP-019, a randomized double-blind, placebo-controlled Phase II screening trial designed to determine if a Phase III trial was warranted for the combination of gemcitabine plus Amplimexon in patients with advanced pancreatic ductal adenocarcinoma of the pancreas. The statistical design required a 40 percent improvement in overall survival, the primary endpoint for a positive outcome. Unfortunately, the results showed no improvement in overall survival for the combination of gemcitabine and Amplimexon.

Protein Identified Which Helps Cancer Cells to Survive Stressful Conditions

http://www.eurekalert.org/pub_releases/2010-07/plos-piw063010.php

Researchers have shown that a protein produced when cells are stressed interacts with a stress sensor allowing cells to survive conditions of intense stress. Understanding this interaction may help scientists interfere with cancer cells so the cells can no longer survive exposure to stressful conditions. Healthy cells are not usually under stress, but unhealthy cells, such as cancer cells, are often under considerable

stress because they grow rapidly in places where they are not supposed to grow. When a cell is under these stressful conditions, the stress protein Hsp70 is activated to help the cell. By understanding more about Hsp70 and the way it functions, scientists can learn how to block its function, allowing unhealthy cells to succumb to stress and die. This could have significant implications in the development of new cancer drugs, which would block the protein to encourage tumor cell death.

U.S. Groups Target 20 Possible Causes of Cancer

<http://www.msnbc.msn.com/id/38266463/ns/health-cancer/>

The American Cancer Society and three federal agencies named 19 chemicals and shift work on Thursday as potential causes of cancer that deserve more investigation. The group published a report with the backing of international experts who said the potential causes they identified had fairly good evidence that they may be a danger and deserved more follow-up. Most are familiar names, such as chloroform, formaldehyde and polychlorinated biphenyls or PCBs, but the list includes indium phosphide, a relatively new compound used in making flat-screen televisions. All have been classified as possible carcinogens by the International Agency for Research on Cancer, the United Nations cancer agency.

Endoscopic Ultrasound Evaluation Associated with Improved Outcomes

http://www.eurekalert.org/pub_releases/2010-07/asfg-eua070810.php

A new study reports that endoscopic ultrasound (EUS) is associated with improved outcomes in patients with localized pancreatic cancer, possibly due to the detection of earlier cancers and improved stage-appropriate management, including more selective performance of curative intent surgery. This is the first study to analyze a large population-based cancer registry and demonstrate that EUS evaluation is associated with improved pancreatic cancer survival.

U.S. Cancer Death Rates Continue to Drop

http://www.nlm.nih.gov/medlineplus/news/fullstory_100815.html

The American Cancer Society reports that U.S. cancer death rates are falling, with big decreases in colon and lung cancer. The improvement was due to a decline in smoking, better treatment and earlier detection. Death rates for all cancer types fell by 2 percent a year from 2001 to 2006 among men and 1.5 percent per year from 2002 to 2006 in women.

Researchers Use Nanoparticles to Shrink Tumors in Mice

<http://www.acor.org/news/display.html?id=9676>

Researchers demonstrated that mesoporous silica nanoparticles (MSNs), tiny particles with thousands of pores, can store and deliver chemotherapeutic drugs in vivo and effectively suppress tumors in mice. The researchers also showed that MSNs accumulate almost exclusively in tumors after administration and that the nanoparticles are excreted from the body after they have delivered their chemotherapeutic drugs. The treatment of mice with camptothecin-loaded MSNs led to shrinkage and regression of xenograft tumors. By the end of the treatment, the mice were essentially tumor free. Mice with breast cancer were used in this study, but the researchers have recently obtained similar results using mice with human pancreatic cancer.

Disclosing a Diagnosis of Cancer: Where and How It Occurs?

<http://www.oncolink.org/news/index.cfm?function=detail&ID=1174>

Cancer patient satisfaction scores are higher when physicians disclose their cancer diagnoses in person, in a personal setting, and spend a substantial amount of time discussing the diagnosis and treatment options, according to research published in the *Journal of Clinical Oncology*. Over 450 cancer patients treated at the NIH's Clinical Center in Bethesda were surveyed about their diagnosis discussion with their physician. The researchers found that 54 percent of 437 respondents said they were told of their diagnosis in person in the physician's office, 18 percent were informed by telephone, and 28 percent in a hospital setting.

European Society for Medical Oncology Publishes Updated Guidelines on Cancer Care

<http://www.acor.org/news/display.html?id=9668>

The European Society for Medical Oncology (ESMO) just released a revised and enhanced set of clinical recommendations designed to help oncologists deliver the best quality care to their patients. The ESMO Clinical Practice Guidelines offer evidence-based information on the incidence of malignancy, diagnostic criteria, staging of disease and risk assessment, treatment plans and follow-up. The guidelines have expanded to include more treatment details and the importance of multidisciplinary plans for particular

patient settings. One new guideline is focused specifically on cardiotoxicity, a potential side-effect of some chemotherapeutic agents. Another guideline on pancreatic cancer includes more detail relating to treatment planning in all disease stages. The new guidelines represent the first stage of a process that will include guidelines for more than 55 different clinical situations, covering almost all tumor types.

Novartis's Afinitor Keeps Pancreatic Neuroendocrine Tumors at Bay Longer

http://www.clinicaspace.com/news_story.aspx?NewsEntityId=185997

Several weeks ago, Novartis Pharmaceuticals revealed their phase III Afinitor® (everolimus) trial in advanced pancreatic cancer. On Thursday, Novartis announced the results of the trial noting that everolimus tablets plus best supportive care more than doubled progression-free survival, or time without tumor growth, versus placebo plus best supportive care in patients with advanced pancreatic neuroendocrine tumors. The study, titled "RADIANT-3," was presented at the 12th World Congress on Gastrointestinal Cancer and is part of the largest clinical trial program in patients with advanced neuroendocrine tumors. Findings from the RADIANT-3 study demonstrated that everolimus extended the median time without tumor growth from 4.6 to 11.0 months when compared with placebo. Additionally, the data showed everolimus reduced the risk of cancer progression by 65%.

Threshold Pharmaceuticals Initiates a Phase 2 Clinical Trial Evaluating TH-302

<http://investor.thresholdpharm.com/releasedetail.cfm?ReleaseID=484212>

Threshold's new trial examines whether gemcitabine versus gemcitabine and TH-302 are effective in the treatment of first-line metastatic pancreatic adenocarcinoma. TH-302 is a drug targeted to activate in the hypoxic regions of tumors. TH-302 consists of two distinct parts: 1) a toxin and 2) a molecular trigger that keeps the toxin inactive until activation by the low oxygen concentration in the tumor environment.

Johns Hopkins Pancreatic Cancer Vaccine Trial - Progress Reported

<http://www.cbsnews.com/stories/2010/06/30/earlyshow/health/main6633634.shtml>

On June 30, the CBS Early Show aired a story about a pancreatic cancer vaccine trial at Johns Hopkins using a vaccine "boost" for disease-free resected patients who were on a prior Hopkins trial. The "boost" trial is no longer enrolling new patients.

AACR-FDA-NCI Cancer Biomarkers Collaborative Consensus Report

<http://clincancerres.aacrjournals.org/content/16/13/3299.full>

The AACR, FDA and NCI created a position statement about advancing the use of biomarkers in cancer drug development. Biomarkers are central to accelerating the identification and adoption of new therapies, but currently, many barriers impede their use in drug development and clinical practice. In 2007, the AACR-FDA-NCI Cancer Biomarkers Collaborative stepped into the national effort to bring together disparate stakeholders to delineate these barriers, to develop recommendations for integrating biomarkers into the cancer drug development, and to implement an action plan to see the promise of biomarkers come to fruition.

Americans are Treated, and Overtreated, to Death

http://news.yahoo.com/s/ap/20100628/ap_on_he_me/us_med_overtreated_final_days

Americans increasingly are treated to death, spending more time in hospitals in their final days, trying last-ditch treatments that often buy only weeks of time, and racking up bills that have made medical care a leading cause of bankruptcies. More than 80 percent of people who die in the U.S. have a long, progressive illness such as cancer, heart failure or Alzheimer's disease. While more than 80 percent of such patients say they want to avoid hospitalization and intensive care when they are dying, the numbers show that's not what is happening. The average time spent in hospice and palliative care is falling because people are starting it too late.

Why Are Blacks More Likely To Die From Cancer Diagnosis?

<http://www.medicalnewstoday.com/articles/193626.php>

Black cancer patients are up to twice as likely as other races to die from their disease. While disparities exist for nearly every common cancer type, the largest differences occur among cancers that benefit most from treatment, according to a review from researchers at the University of Michigan Comprehensive Cancer Center. The researchers attributed these disparities to three factors including patients, underuse of care, and hospital systems.

Get Moving: Cancer Survivors Urged to Exercise

<http://www.msnbc.msn.com/id/37978604/ns/health-cancer/>

New guidelines urge cancer survivors to exercise even for those who have not yet finished their treatment. There is growing evidence that physical activity improves quality of life and eases some cancer-related fatigue. Moreover, it can help fend off a serious decline in physical function that can last long after therapy is finished. The American College of Sports Medicine convened a panel of cancer and exercise specialists to evaluate the evidence. Guidelines issued this month advise cancer survivors to aim for the same amount of exercise as recommended for the average person: about 2½ hours a week. Patients still in treatment may not feel up to that much, the guidelines acknowledge, but should avoid inactivity on their good days.

How Dietary Supplement May Block Cancer Cells

<http://www.acor.org/news/display.html?id=9648>

Researchers at the Ohio State University Comprehensive Cancer Center have discovered how a substance that is produced when eating broccoli and brussel sprouts can block the proliferation of cancer cells. The substance, indole-3-carbinol (I3C), may have anticancer effects and other health benefits. The findings show how I3C affects cancer cells and normal cells. The laboratory and animal study discovered a connection between I3C and a molecule called Cdc25A, which is essential for cell division and proliferation.

Cancer Docs 'Frustrated' By Lack of Useful Info in Journal Articles

http://www.nlm.nih.gov/medlineplus/news/fullstory_101379.html

According to a study reported by University of Florida researchers, medical journals should include more clinical details in cancer research studies to help doctors better understand and utilize results. They analyzed 262 articles published from 2005 to 2008 in the *Journal of Clinical Oncology*, *The New England Journal of Medicine*, the *Journal of the National Cancer Institute*, and the journals *Cancer* and *Blood*. Only 11 percent of the articles offered all the information required by doctors to prescribe and monitor new cancer therapies. According to the researchers, adding more practical data from clinical trials would help physicians and patients.

Cancer-Metabolism Link Runs Deep in Humans

<http://www.acor.org/news/display.html?id=9713>

Eighty years ago, the medical establishment believed cancer was caused by a dysfunction of metabolism, but the idea went out of vogue. Now, scientists are again looking at metabolism and its role in cancer and other common diseases. Metabolism is a highly connected network of reactions that are arranged in parallel and interacting pathways. Such parallelism can mask how genes are linked with disease traits and make it difficult to treat conditions. Researchers at Harvard Medical School and Boston University analyzed ways to "break" the multiple parallel pathways of a metabolic network. Their research suggests that the many pathways in the human metabolic network buffer each other to a striking degree.

Asthma and Eczema Sufferers Have Lower Cancer Risk

<http://www.acor.org/news/display.html?id=9710>

Men with a history of asthma or eczema generally had a lower risk of developing cancer, according to a study carried out by French researchers. Asthma and eczema are allergies brought about by a hyper-reactive immune system which might have enabled abnormal cells to have been eliminated more efficiently, thereby reducing the risk of cancer. Although the study did not identify which specific factors that are related to asthma and eczema were responsible for reducing the risk of cancer, it offers new angles for research into the molecular and immunological mechanisms that are involved and offers a potential strategy for cancer prevention.

Researchers use Nanoparticles as Destructive Beacons to Zap Tumors

<http://www.acor.org/news/display.html?id=9717>

Wake Forest University Baptist Medical Center researchers are developing a way to treat cancer by using lasers to light up tiny nanoparticles and destroy tumors with the ensuing heat. They presented their work at the American Association of Physicists in Medicine meeting, describing their technology as iron-containing multi-walled carbon nanotubes (MWCNTs), which are threads of hollow carbon that are 10 thousand times thinner than a human hair. In laboratory experiments, the researchers showed that by using an MRI scanner, they could image these particles in living tissue, watch as they approached a tumor, zap them with a laser, and destroy the tumor in the process.

Novel Therapies for Pancreatic Cancer

<http://www.futuremedicine.com/doi/pdf/10.2217/fon.10.70>

Despite the setbacks encountered with a number of targeted agents in pancreatic cancer, steady improvements have been achieved over the years in our understanding of the biology of pancreatic cancer and the development of novel therapeutic strategies. A number of genetically targeted agents have shown encouraging results in the laboratory, although a major obstacle would be the availability of an efficient and sustained delivery system in humans.

Abstracts

High Levels of Nucleolar Expression of Nucleolin

<http://clincancerres.aacrjournals.org/content/16/14/3734.abstract>

Nucleolin is a major nucleolar protein that has been shown to be overexpressed in rapidly dividing cells and plays an essential role in cell proliferation and survival. However, the expression and significance of nucleolin in pancreatic ductal adenocarcinoma (PDA) have not been studied. Together with his colleagues, Dr. Huamin Wang, recipient of the 2007 Skip Viragh – Pancreatic Cancer Action Network – AACR Career Development Award, used a tissue microarray consisting of 1.0-mm cores of tumor and paired nonneoplastic pancreatic tissue from 69 pancreaticoduodenectomy specimens with stage II PDA. Nucleolin expression was evaluated by immunohistochemistry and scored quantitatively by image analysis. Nucleolin expression was classified as nucleolin-high or nucleolin-low using the median nucleolin labeling index of 3.5% as cutoff. Staining results were correlated with clinicopathologic features and survival. The results indicated that nucleolin was overexpressed in PDAs and PDA cell lines. A high level of nucleolar expression of nucleolin was an independent prognostic marker for better survival for patients with stage II PDAs.

Occupational Exposures and Risk of Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20640489>

The study analyzed the relationship between occupation (and specific occupational exposures) and risk of exocrine pancreatic cancer. Cases with ductal adenocarcinoma were more likely to have been exposed to chlorinated hydrocarbon solvents. Researchers also observed significant associations with exposure to 'synthetic polymer dust exposure' and 'ionizing radiation'. Suggestive increases in risk were observed for 'pesticides', 'diesel and gasoline engine exhaust', and 'hydrocarbon solvents'. Results support the hypothesis that occupational exposure to chlorinated hydrocarbon solvents is associated with exocrine pancreatic cancer.

Detection of Liver Metastases Secondary to Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20635101>

The combination of computed tomography during arterial portography and computed tomography-assisted hepatic arteriography is useful to confirm liver metastases and can potentially offer more accurate staging of pancreatic cancer compared with multidetector computed tomography.

Fructose Induces Transketolase Flux to Promote Pancreatic Cancer Growth

<http://www.ncbi.nlm.nih.gov/pubmed/20647326>

Carbohydrate metabolism via glycolysis and the tricarboxylic acid cycle is pivotal for cancer growth, and increased refined carbohydrate consumption adversely affects cancer survival. Traditionally, glucose and fructose have been considered as interchangeable monosaccharide substrates that are similarly metabolized, and little attention has been given to sugars other than glucose.

New Strategies in Pancreatic Cancer: Emerging Epidemiological and Therapeutic Concepts

<http://www.ncbi.nlm.nih.gov/pubmed/20647474>

The article reviews findings that present new avenues for understanding the etiology of pancreatic cancer and opportunities for developing novel strategies for prevention and treatment of it.

Clinicopathologic Analysis of Surgically Proven Intraductal Papillary Mucinous Neoplasms

<http://www.ncbi.nlm.nih.gov/pubmed/20640860>

The main pancreatic duct diameter is a significant predictor for malignancy and invasiveness. Therefore, IPMN patients with main pancreatic duct dilatation (>5 mm) should be considered surgical resection.

Phase I Study of Cetuximab as a Radiosensitizer with Chemoradiation

<http://www.ncbi.nlm.nih.gov/pubmed/20589377>

The study assessed the safety of cetuximab with concurrent gemcitabine and abdominal radiation in the treatment of patients with locally advanced adenocarcinoma of the pancreas. Results show that this combined treatment can be safely administered in locally advanced pancreatic cancer but exhibited limited activity.

Helical Tomotherapy with Concurrent Capecitabine for the Treatment of Inoperable Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20582394>

The study evaluated the feasibility and clinical outcome of concurrent administration of capecitabine with tomotherapy in patients with advanced pancreatic cancer. Treatment was well tolerated with only minor toxicities. The study showed tomotherapy with concurrent capecitabine is a feasible option without significant toxicities in patients with advanced pancreatic cancer.

A Neoadjuvant Strategy for Pancreatic Adenocarcinoma Increases Likelihood of Receiving all Components of Care

<http://www.ncbi.nlm.nih.gov/pubmed/20590888>

Recent studies have shown adjuvant therapy improves outcomes from pancreatic cancer. This study investigates receipt and timing of pancreatic cancer treatments, and association with outcomes. The study showed that after resection, a substantial proportion of patients do not receive adjuvant therapy, and have worse survival. In this study, neoadjuvant treatment increased both the proportion of patients receiving all components of recommended therapy and the R0 resection rate.

Preoperative Body Composition is Influenced by Stage of Operable Pancreatic Adenocarcinoma but Does Not Predict Survival After Whipple

<http://www.ncbi.nlm.nih.gov/pubmed/20590908>

Few studies have investigated cachexia's influence on long-term survival in patients with operable tumors. This study reports that pancreatic cancer patients undergoing a Whipple have reduced body fat and total body potassium compared with community controls, while those with stage III tumors had greater deficits of fat, total body potassium and protein stores. However, preoperative body composition was a poor predictor of postoperative survival after pathological data were considered.

Volumetric Modulated Arc Therapy for Advanced Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20582394>

Intensity-modulated radiotherapy (IMRT) allows for improved sparing of organs at risk in advanced pancreatic cancer. The study evaluated if volumetric modulated arc therapy (RapidArc [RA]) could be used as an alternative to IMRT in such cases.

Cucurbitacin B, a Novel in Vivo Potentiator of Gemcitabine with Low Toxicity

<http://www.ncbi.nlm.nih.gov/pubmed/20590594>

The anti-tumor effects and toxicities of cucurbitacin B in combination with gemcitabine were tested against human pancreatic cancer cells in a murine xenograft model. Results show the combination of cucurbitacin B and gemcitabine had profound anti-proliferative effects in vivo against xenografts of human pancreatic cancer cells, without any significant signs of toxicity. The researchers conclude this combination should be examined in therapeutic trials of pancreatic cancer.

The Incidence and Outcomes of Pancreatectomy in Patients with Metastatic Pancreatic Adenocarcinoma

<http://www.ncbi.nlm.nih.gov/pubmed/20601808>

A large number of patients from Los Angeles County have undergone pancreatic resection despite the presence of known metastatic disease. Patient survival remains abysmal in this setting and these results are likely a microcosm of the surgical management of metastatic pancreatic cancer in the U.S. These results highlight the necessary efforts to maintain appropriate standards of care in the management of pancreatic cancer.

Phase III Study of Gemcitabine Plus Cetuximab Versus Gemcitabine: Directed Intergroup Trial S0205

<http://jco.ascopubs.org/cgi/content/abstract/JCO.2009.25.7550v1>

In patients with advanced pancreas cancer, the anti-EGFR monoclonal antibody cetuximab did not improve the outcome compared with patients treated with gemcitabine alone. Alternate targets other than EGFR should be evaluated for new drug development.

Pain and Emotional Well-Being Outcomes in Southwest Oncology Group: Directed Intergroup Trial S0205

<http://jco.ascopubs.org/cgi/content/abstract/JCO.2009.25.8285v1>

Researchers observed palliated pain and improved well-being for patients on this trial. However, these improvements were similar in both treatment arms, suggesting that the addition of cetuximab did not contribute to improvement in these health-related quality of life outcomes.

Metronomic Gemcitabine in Combination with Sunitinib Inhibits Multisite Metastasis and Increases Survival in Orthotopic Model of Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20606044>

Metronomic chemotherapy suppresses growth of primary tumors and established metastases. However, its effect on metastatic progression is essentially unknown. Researchers report on the treatment of a metastatically competent model of pancreatic cancer with metronomic gemcitabine and sunitinib, discussing the potential of this therapeutic paradigm against pancreatic cancer in the adjuvant and maintenance settings.

Elevated Neutrophil to Lymphocyte Ratio Predicts Survival in Advanced Pancreatic Cancer

<http://www.ncbi.nlm.nih.gov/pubmed/20602543>

Elevated neutrophil to lymphocyte ratio is a predictor of shorter survival in patients with advanced pancreatic cancer.

Pancreatic Cancer Risk Counseling and Screening

<http://www.ncbi.nlm.nih.gov/pubmed/20623197>

Participation in a pancreatic cancer screening program does not lead to a significant increase in risk perception, cancer worry, or general distress. Participants with high baseline levels of risk perception and distress may benefit from a more comprehensive risk assessment and psychological support.

Assessing the Volume-Outcome Hypothesis and Region-Level Quality Improvement Interventions

<http://www.ncbi.nlm.nih.gov/pubmed/20625843>

Regionalization was associated with improved operative mortality in Ontario but not in Quebec, undermining the volume-outcome hypothesis. The Ontario quality improvement interventions likely were of little influence since patterns in regionalization and operative mortality were similar before and after year 1999.

Mayo Clinic Experience with Very Rare Exocrine Pancreatic Neoplasms

<http://www.ncbi.nlm.nih.gov/pubmed/20622706>

The overall survival of all patients with very rare, exocrine pancreatic neoplasm was better than matched controls, but no statistical difference was seen between the groups with stage 4 disease.