

LE Magazine June 2003

ABSTRACTS

Progesterone

A placebo-controlled trial of long-term oral combined continuous hormone replacement therapy in postmenopausal women: effects on arterial compliance and endothelial function.

OBJECTIVE: To study the effects of long-term combined continuous oral hormone replacement therapy (HRT) on vascular function in healthy postmenopausal women. **BACKGROUND:** The cardiovascular effects of HRT are controversial. Improvement in vascular function is a proposed mechanism of estrogen action but there are no long-term controlled human trials in this area. In this study, we examined the effects of HRT on lipid profiles and vascular function, encompassing both biomechanical arterial properties [systemic arterial compliance (SAC) and pulse wave velocity (PWV)] and endothelial function [flow-mediated vasodilation (FMD)]. **METHODS:** In this two-year, double-blind, placebo-controlled study, 59 healthy postmenopausal women were randomized to oral combined continuous estrogen and progesterone [Kliogest, estradiol (2 mg), norethisterone (1 mg)] or placebo, with end-points measured at baseline, six weeks and after 6, 12 and 24 months of treatment. **RESULTS:** Oral combined HRT reduced lipoprotein a [Lp(a)], although other lipid benefits were not observed. There were no significant changes in SAC, PWV or FMD with oral combined HRT, compared to placebo. **CONCLUSION:** In this long-term, randomized placebo-controlled trial, oral continuous HRT with combined estradiol and norethisterone in healthy postmenopausal women did not improve a spectrum of indices of arterial function compared to placebo. These results suggest that HRT might not be of cardiovascular benefit in postmenopausal women.

Clin Endocrinol (Oxf) 2001 Nov;55(5):673-8

Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss.

OBJECTIVE: To determine effectiveness of transdermal progesterone cream for controlling vasomotor symptoms and preventing postmenopausal bone loss. **METHODS:** We randomly assigned 102 healthy women within five years of menopause to transdermal progesterone cream or placebo. Study subjects and investigators were masked until data analysis was completed. An initial evaluation included complete history, physical examination, bone mineral density determination and serum studies (TSH, FSH, lipid profile and chemistry profile). Subjects were instructed to apply a quarter teaspoon of cream (containing 20 mg progesterone or placebo) to the skin daily. Each woman received daily multivitamins and 1200 mg of calcium and were seen every four months for review of symptoms. Bone scans and serum chemistries were repeated after one year. **RESULTS:** Thirty of the 43 (69%) in the treatment group and 26 of the 47 (55%) in the placebo group complained initially of vasomotor symptoms. Improvement or resolution of vasomotor symptoms, as determined by review of weekly symptom diaries, was noted in 25 of 30 (83%) treatment subjects and five of 26 (19%) placebo subjects ($P < .001$). However, the number of women who showed gain in bone mineral density exceeding 1.2% did not differ ($\alpha = .05$, power of 80%). **CONCLUSION:** Although we found no protective effect on bone density after one year, we did see a significant improvement in vasomotor symptoms in the treated group.

Obstet Gynecol 1999 Aug;94(2):225-8

Effects of acute administration of natural progesterone on peripheral vascular responsiveness in healthy postmenopausal women.

Peripheral vascular responses to acute administration of natural progesterone were studied in 12 postmenopausal women (mean \pm SD age 50.3 \pm 4.8 years) with no evidence of cardiovascular disease. According to a randomized, double-blind protocol, all subjects were given natural progesterone as a vaginal cream, able to produce a rapid peak and decay of plasma hormone concentrations, or matched placebo, with crossover after a one-week washout period. Forearm blood flow and peak flow after ischemic stress (ml/100 ml/min), local vascular resistance (mm Hg/ml/100 ml/min), venous volume (ml/100 ml), and venous compliance (ml/100 ml/mm Hg) were measured by strain-gauge venous occlusion plethysmography at baseline and after progesterone or placebo administration. Plasma norepinephrine concentrations were determined by high-performance liquid chromatography with electrochemical detection. Progesterone sharply decreased forearm blood flow ($p < .01$) through an increase in local vascular resistance ($p < .01$). Measures of venous function remained unchanged. Although the hormone increased circulating norepinephrine concentrations ($p < .05$), there were no significant changes in mean arterial pressure or heart rate. Furthermore, progesterone reduced the local vasodilator capacity, shown by a decrease in forearm delta flow (difference between peak flow and basal flow, $p < .05$). Compared with the well-known effect of estrogen, progesterone exerted an opposite action on peripheral vascular responsiveness. Peripheral circulatory changes may be attributed to a direct activity of

progesterone on the arterial wall and may in part reflect a modulation of the hormone on peripheral sympathetic tone. Consideration must be given to the hypothesis that the addition of progestin may attenuate the beneficial effects of unopposed estrogen replacement therapy in postmenopausal women.

Am J Cardiol 1999 Jul 15;84(2):214-8

Effects of estrogen and progesterone on age-related changes in arteries of postmenopausal women.

1. Hormone replacement therapy (HRT) with estrogen or estrogen plus progestin may have different effects on arterial structure and function. To examine this question, carotid artery intima-medial thickness (IMT) and indices of systemic and carotid arterial compliance were measured in groups of older men, postmenopausal women not on HRT (non-HRT) and those women on long-term HRT with estrogen alone (HRT-E) or oestrogen plus progestin (HRT-EP). 2. Sixty men, 90 postmenopausal women taking HRT and 91 not taking HRT participated in the study. The groups were similar for age, body mass index, numbers of smokers, physical activity, alcohol intake and blood pressure. 3. Plasma total cholesterol was reduced and high-density lipoprotein-cholesterol was increased in the HRT group compared with the non-HRT group; low-density lipoprotein-cholesterol, triglyceride and lipoprotein (a) values were similar in these two groups. Results for HRT-E and HRT-EP subgroups were similar. 4. Carotid IMT was significantly reduced in the HRT group compared with men and non-HRT groups. Results for HRT-E and HRT-EP subgroups were similar. 5. Mean systemic arterial compliance (SAC) was significantly greater in men than in women and was related to age; SAC was higher in both HRT-E and HRT-EP groups compared with the non-HRT group. Indices of carotid stiffness were similar in men and in non-HRT groups. The HRT-EP group showed increased carotid stiffness compared with the HRT-E group. 6. There is an apparent protective effect of long-term estrogen therapy on carotid IMT and age-related changes in arterial stiffness. Progestin does not alter the IMT effects but may adversely influence arterial stiffness.

Clin Exp Pharmacol Physiol 1997 Jun;24(6):457-9

Transition of ovarian arterial compliance during the human menstrual cycle, assessed by Doppler ultrasound-correlation with serum hormone levels.

Ovarian arterial velocimetry was performed using color and pulsed Doppler ultrasound. Seventy-one examinations were done on nine healthy women with regular menstrual cycles. The change in ovarian arterial compliance was based on the calculation of the pulsatility index (PI). In the active ovary carrying a dominant follicle or corpus luteum, PI in the early proliferative phase was significantly higher than that in the late proliferative phase (p less than 0.001), and PI in the early secretory phase was significantly lower than that in the late proliferative phase (p less than 0.001). PI became significantly higher in the late secretory phase than that in the early secretory phase (p less than 0.001). In the inactive ovary without a follicle or corpus luteum, no changes were seen among the values for PI, in any menstrual phase. There was a significant difference between the values for PI in the active ovary and the inactive ovary in the late proliferative, the early and the late secretory phases (p less than 0.001), respectively. The PI values for the active ovary significantly correlated with the serum progesterone levels ($r = -0.53$, p less than 0.05) but not with the estradiol levels. These findings provide a useful foundation for assessing ovarian hemodynamics during the menstrual cycle.

Nippon Sanka Fujinka Gakkai Zasshi 1990 Jul;42(7):662-6

Estrogen and thyroid hormone receptor interactions: physiological flexibility by molecular specificity.

The influence of thyroid hormone on estrogen actions has been demonstrated both in vivo and in vitro. In transient transfection assays, the effects of liganded thyroid hormone receptors (TR) on transcriptional facilitation by estrogens bound to estrogen receptors (ER) display specificity according to the following: 1) ER isoform, 2) TR isoform, 3) the promoter through which transcriptional facilitation occurs and 4) cell type. Some of these molecular phenomena may be related to thyroid hormone signaling of seasonal limitations upon reproduction. The various combinations of these molecular interactions provide multiple and flexible opportunities for relations between two major hormonal systems important for neuroendocrine feedbacks and reproductive behaviors.

Physiol Res 2002 Oct;82(4):923-44

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ABSTRACTS

Ovarian aging and the menopausal transition.

The underlying cause of the menopausal transition is a dwindling supply of FSH-responsive follicles available for ovulation. Additional factors may include dysregulation of existing follicles and concurrent follicle and oocyte deficits that may be strictly anatomic or consequences of the hormonal milieu. In the early transition, menstrual irregularity is infrequent but cycle length shortens by one to four days. Estrogen production may be overall elevated, even in ovulatory cycles. As anovulatory cycles become more common, and amenorrhoea of greater duration, evidence of impaired hypothalamic-pituitary function is present. Estradiol has been implicated as an agent responsible for the impaired positive feedback response. A model of the early menopausal transition suggests that the loss of FSH restraint by the inhibins, due to a critically diminished follicle pool, is the early event that precedes overt follicle failure and may initiate intervals of hyperoestrogenaemia. The hormonal fluctuations in the early and late menopausal transition may account for some of the signs and symptoms seen during these phases.

Best Pract Res Clin Obstet Gynaecol 2002 Jun;16(3):263-76

Progesterone receptor activation: An alternative to SERMs in breast cancer.

Data regarding the effects of progesterone and a progestagen on human normal breast epithelial cell proliferation and apoptosis are presented here. In postmenopausal women, adding progesterone to percutaneously administered estradiol significantly reduces the proliferation induced by estradiol. In vitro and in premenopausal women, stopping the administration of noregestrol acetate triggers a peak of apoptosis. Fibro-adenoma and cancerous cells do not show this regulation of apoptosis. Progesterone seems to be important in normal breast homeostasis.

Eur J Cancer 2000 Sep;36 Suppl 4:S90-1

Menses and breast cancer: does timing of mammographically directed core biopsy affect outcome?

BACKGROUND AND OBJECTIVES: Studies have shown molecular, genetic and cellular changes in breast cancer during the menstrual cycle. Changes in proliferative and metastatic potential of breast cancer cells during menses could explain improved survival when tumors are surgically removed in the luteal phase. This study examined if timing of mammography/core biopsy (MAM-CB) also affected breast cancer prognosis (histological tumor grade). **METHODS:** Eighty-five premenopausal women undergoing MAM-CB at one clinic between March 1995 and February 1998 were retrospectively studied. All patients had Stage I or II breast cancer surgically treated. Patients were grouped by phase of menses at MAM-CB: follicular (F, Days 0-14) or luteal (L, Days 15-35). Groups were comparable in age, menarche, family history, nulliparity, breastfeeding and total percentage of clinically palpable tumors. Pathological characteristics of the tumors (tumor size, tumor type, estrogen and progesterone receptor status, axillary lymph node status, the presence of lymphatic or vascular invasion and extranodal metastasis) was also comparable across the two groups. **RESULTS:** Low-grade tumors were more frequent in the MAM-CB group L, whereas high-grade tumors were more common in the MAM-CB group F ($P = 0.002$, $\chi^2(4) = 17.06$). **CONCLUSIONS:** Timing of MAM-CB in relation to menses may be a factor influencing breast cancer outcome. Future studies examining the effect of menses on the outcome of breast cancer should consider the potential effect of the timing of MAM-CB.

J Surg Oncol 2000 Jul;74(3):232-6

Timing of surgery during the menstrual cycle and prognosis of breast cancer.

There are conflicting reports on the differential effect of surgery performed during the two phases of the menstrual cycle, namely, follicular and luteal and prognosis of operable breast cancer. A statistical meta-analysis of the published evidence suggests a modest survival benefit of 15+/-4% when the operation is performed during the luteal phase. Further research in this area might provide a novel avenue to understand the natural history of breast cancer. A spin off from these studies might be the understanding of the importance of events that occur at the time of surgery in determining long term prognosis.

J Biosci 2000 Mar;25(1):113-20

Osteoarthritis: diagnosis and therapeutic considerations.

Osteoarthritis is a common rheumatologic disorder. It is estimated that 40 million Americans and 70% to 90% of persons older than

75 years are affected by osteoarthritis. Although symptoms of osteoarthritis occur earlier in women, the prevalence among men and women is equal. In addition to age, risk factors include joint injury, obesity, and mechanical stress. The diagnosis is largely clinical because radiographic findings do not always correlate with symptoms. Knowledge of the etiology and pathogenesis of the disease process aids in prevention and management. Acetaminophen and nonsteroidal anti-inflammatory medications remain first-line drugs. Agents such as cyclooxygenase-2 inhibitors and sodium hyaluronate joint injections offer new treatment alternatives. Complementary medication use has also increased. Therapeutic goals include minimizing symptoms and improving function.

Am Fam Physician 2002 Mar 1;65(5):841-8

A critical evaluation of side effect data on COX-2 inhibitors.

BACKGROUND: Celecoxib and rofecoxib have been used in Norway since 2000. These cyclooxygenase 2 inhibitors (COX-2 inhibitors) have no better clinical efficacy than older non-steroid anti-inflammatory drugs (NSAIDs) in the treatment of rheumatoid arthritis or osteoarthritis, but may possibly lead to a lower incidence of upper gastrointestinal ulcers. **MATERIAL AND METHODS:** Published and unpublished clinical data on side effects were examined and interpreted. The aim was to evaluate the general safety of these new drugs compared with older NSAIDs. **RESULTS:** The incidence of side effects is addressed in two large published studies comparing COX-2 inhibitors with other NSAIDs. Only rofecoxib showed an unequivocal lower incidence of complicated upper gastrointestinal ulcers. However, the incidence of serious side effects was significantly higher in the rofecoxib group. In the other study there was a trend towards more serious side effects in the celecoxib group. **INTERPRETATION:** The available clinical data do not suggest that COX-2 inhibitors are safer drugs than other NSAIDs.

Tidsskr Nor Laegeforen 2002 Feb 20;122(5):476-80

Prevalence of cardiovascular disease risk factors among US adults with self-reported osteoarthritis: data from the Third National Health and Nutrition Examination Survey.

OBJECTIVE: To estimate the prevalence of traditional risk factors for cardiovascular disease (CVD) among U.S. adults with osteoarthritis (OA). **METHODS:** Using survey data from the Third National Health and Nutrition Examination Survey, we estimated the prevalence of selected CVD risk factors among a U.S. OA and nonarthritic adult population. In additional analyses, we stratified the sample by gender and age (35-44, 45-64, and 65+ years) to further understand the CVD risk profile in an arthritic population and nonarthritic population. Relevant data on each survey participant's demographics, arthritis status, CVD risk factors, and sampling weights were obtained from the survey database. **RESULTS:** Of the 115.9 million US adults aged \geq 35 years, 24.3 million (21%) have OA. Hypertension is prevalent in approximately 40% of OA patients; 20% of the patients smoke and 11% have diabetes. Prevalence of high total cholesterol is estimated to be 32%, while prevalence of low high-density lipoprotein cholesterol is estimated at 13%. Approximately 37% of OA patients are estimated to have renal impairment, but less than 1% suffer from renal failure. **CONCLUSION:** National survey data suggest that, on average, U.S. adults with OA have a high prevalence of cardiovascular risk factors. These findings highlight the need to consider patients' comorbidities when selecting the appropriate treatment options.

Am J Manag Care 2002 Oct;8(15 Suppl):S383-91

Etiology, pathophysiology and conservative therapy of degenerative rheumatic diseases.

ETIOLOGY OF DEGENERATIVE JOINT DISEASES: Etiology of degenerative joint diseases is still not clearly understood and there is no specific management for this group of diseases. Various pathological conditions cause damage of the articular cartilage and lead to clinically and radiographically recognized impairment. Biomechanical, metabolic, genetic factors, inflammation and other risk factors contribute to development of osteoarthrosis. **PATHOPHYSIOLOGY OF DEGENERATIVE JOINT DISEASES:** Osteoarthrosis is characterized by progressive erosion of articular cartilage and bone overgrowth at the joint margins. Cartilage integrity requires balance between synthesis and degradation of matrix components. Chondrocytes react to various mechanical and chemical stresses in order to stabilize and restore the tissue. Failures in stabilizing and restoring the tissue lead to cartilage degeneration that may be irreversible. For better understanding of conservative management of degenerative joint diseases it is important to know the impact of pathophysiology mechanisms on development of degenerative joint diseases. There is great variability in the rate of progression of erosive processes in articular cartilage in clinical, radiographic signs and course of the disease. This is in relation with many factors, as well as with management and response to therapy. **TREATMENT OF DEGENERATIVE JOINT DISEASES:** Treatment should vary depending on the severity of disease and patient's expectations and level of activity. Besides analgesic and anti-inflammatory drugs, conventional and not conventional treatment and techniques can be used for management of osteoarthrosis. Physical therapy and exercises are very important for maintaining muscle strength, joint stability and mobility, but should be closely monitored for optimal efficacy.

Med Pregl 2002 Jan-Feb;55(1-2):35-9

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ABSTRACTS

SAMe

Chemoprevention of hepatocarcinogenesis: S-adenosylmethionine.

Accumulation of genetic changes characterizes the progression of cells, initiated by carcinogens, to full malignancy. Various epigenetic mechanisms, such as high polyamine synthesis, aberrant DNA methylation, and production of reactive oxygen species, may favor this process by stimulating growth and inducing DNA damage. We observed a decrease in S-adenosylmethionine (SAMe) content in the liver, associated with DNA hypomethylation in rat liver, during the development of preneoplastic foci, and in neoplastic nodules and hepatocellular carcinomas, induced in diethylnitrosamine-initiated rats by "resistant hepatocyte" (RH) protocol. Reconstitution of the methyl donor level in the liver by SAMe administration inhibits growth and induces phenotypic reversion and apoptosis of preneoplastic cells. A six-month SAMe treatment results in a sharp and persistent decrease in development of neoplastic nodules, suggesting a long duration of SAMe chemopreventive effect. Various observations support the suggestion of a role of DNA methylation in chemoprevention by SAMe: (1) Exogenous SAMe reconstitutes the SAMe pool in preneoplastic and neoplastic liver lesions. (2) DNA methylation is positively correlated with SAMe:S-adenosylhomocysteine (SAH) ratio in these lesions. (3) 5-Azacytidine, a DNA methyltransferase inhibitor, inhibits chemoprevention by SAMe. (4) c-Ha-ras, c-Ki-ras, and c-myc are hypomethylated and overexpressed in preneoplastic liver. Their expression is inversely correlated with SAM:SAH ratio in SAMe-treated rats. (5) S-Adenosyl-L-methionine treatment results in overall DNA methylation and partial methylation of these genes. Other possible mechanisms of SAMe treatment include inhibition of polyamine synthesis, linked to partial transformation of SAMe into 5'-methylthioadenosine (MTA), and antioxidant and antifibrogenic activities of both SAMe and MTA.

Alcohol 2002 Jul;27(3):193-8

S-Adenosylmethionine and mitochondrial reduced glutathione depletion in alcoholic liver disease.

The pathogenesis of alcohol-induced liver disease is not well understood, and many factors have been described to contribute to the progressive loss of liver functions, including the overgeneration of reactive oxygen species. Mitochondria are specific targets of the toxic effects of ethanol, reflected in the loss of phosphorylative oxidation and defective ATP generation, which underlie one of the hallmarks of the hepatic alterations induced by chronic alcohol intake. Mitochondrial reduced glutathione (GSH), whose primary function is to maintain a competitive functional organelle, becomes depleted by alcohol intake. Furthermore, GSH depletion in hepatocyte mitochondria has been revealed as an important mechanism in the sensitization of liver to alcohol-induced injury. This depletion of the mitochondrial GSH level is determined by an impaired transport of GSH from the cytosol into the mitochondrial matrix owing to a partial inactivation of mitochondrial GSH carrier. The loss of function of this specific mitochondrial transporter is due to the alterations in the physicochemical properties of the inner mitochondrial membrane caused by alcohol. Because of the primary defect in the transport of cytosolic GSH into mitochondria, GSH precursors are inefficient in replenishing the levels of mitochondrial GSH despite significant increase in cytosolic GSH. Supplementation of S-adenosylmethionine (SAMe) to rats fed alcohol chronically has been shown to replete the mitochondrial GSH levels because of normalization of the microviscosity of the mitochondrial inner membrane. Because of the instrumental role of GSH in mitochondria in hepatocyte survival against inflammatory cytokines, its repletion by SAMe feeding may underlie the potential therapeutic use of this hepatoprotective agent in the treatment of alcohol-induced liver injury.

Alcohol 2002 Jul;27(3):179-83

Liver in sepsis and systemic inflammatory response syndrome.

In patients with sepsis and SIRS, the liver has two opposing roles: a source of inflammatory mediators and a target organ for the effects of the inflammatory mediators. The liver is pivotal in modulating the systemic response to severe infection, because it contains the largest mass of macrophages (Kupffer cells) in the body; these macrophages can clear the endotoxin and bacteria that initiate the systemic inflammatory response. This article summarizes the functional changes that take place in the liver during sepsis and systemic inflammatory response syndrome and discusses the cellular and molecular mechanisms that underlie clinical outcomes.

Clin Liver Dis 2002 Nov;6(4):1045-66, x

SARS

Rhinovirus and coronavirus infection-associated hospitalizations among older adults.

Rhinoviruses and coronaviruses are recognized as the major causes of the common cold syndrome. The role of these viruses in more serious respiratory illnesses resulting in hospitalization is less well defined. During a winter when influenza A infection was prevalent, 100 elderly adults hospitalized because of cardiopulmonary illnesses were evaluated for rhinovirus and coronavirus infection. Patients who tested negative for influenza or respiratory syncytial virus had nasal swab samples tested for rhinovirus, coronavirus OC43, and coronavirus 229E by reverse-transcription polymerase chain reaction and for coronaviruses by serologic testing. Twelve percent of patients had rhinovirus or coronavirus identified (rhinovirus, four patients; coronavirus 229E, four patients; coronavirus OC43, three patients; and mixed rhinovirus/coronavirus 229E infection, one patient). All patients had significant underlying diseases. Although all patients recovered, the mean length of stay was eight days; four persons had pneumonia, and one required ventilator support. These data suggest that rhinoviruses and coronaviruses may be associated with serious respiratory illnesses in frail older adults.

J Infect Dis 2002 May 1;185(9):1338-41

Coronavirus infections of man associated with diseases other than the common cold.

About 14,000 paired sera, from patients with various types of acute infectious diseases with suspected viral origin, were screened by complement fixation against a wide set of viral antigens, including coronavirus OC43. A significant change in OC43 antibodies was recorded in 33 cases and a constant high titre, defined as a titre occurring in the respective age group in less than 1% of all sera examined, was found in 45 cases. On the basis of careful retrospective analysis of hospital case records it was concluded that in 28 cases with an increase of OC43 antibody titres, and in two with titre decrease, a disease could be associated with an acute coronavirus infection. In 16 cases the disease was dominated by respiratory symptoms. Eight of these patients, four children and four adults, had pneumonia. Three of the eight pneumonia patients had, however, another concomitant infection, too. Four patients had neurological symptoms, one had severe perimyocarditis, and in five cases fever was the only symptom recorded. Among the patients with a statistically significant high titre of OC43 antibodies, there were 14 cases where a suggestive association with a disease could be envisaged on the basis of hospital records. Five of these patients had pneumonia. These results suggest that human coronaviruses, so far considered only as one group of causative agents of the common cold, may also be associated with other and more severe diseases in all age groups.

J Med Virol 1980;6(3):259-65

Identification of Severe Acute Respiratory Syndrome in Canada.

BACKGROUND: Severe Acute Respiratory syndrome (SARS) is a condition of unknown cause that has recently been recognized in patients in Asia, North America and Europe. This report summarizes the initial epidemiologic findings, clinical description, and diagnostic findings that followed the identification of SARS in Canada. **METHODS:** SARS was first identified in Canada in early March 2003. We collected epidemiologic, clinical and diagnostic data from each of the first 10 cases prospectively as they were identified. Specimens from all cases were sent to local, provincial, national, and international laboratories for studies to identify an etiologic agent. **RESULTS:** The patients ranged from 24 to 78 years old; 60 percent were men. Transmission occurred only after close contact. The most common presenting symptoms were fever (in 100% of cases) and malaise (in 70%), followed by nonproductive cough (in 100%) and dyspnea (in 80%) associated with infiltrates on chest radiography (in 100 percent). Lymphopenia (in 89% of those for whom data were available), elevated lactate dehydrogenase levels (in 80%), elevated aspartate aminotransferase levels (in 78%), and elevated creatinine kinase levels (in 56%) were common. Empirical therapy most commonly included antibiotics, oseltamivir, and intravenous ribavirin. Mechanical ventilation was required in five patients. Three patients died, and five have had clinical improvement. The results of laboratory investigations were negative or not clinically significant except for the amplification of human metapneumovirus from respiratory specimens from five of nine patients and the isolation and amplification of a novel coronavirus from five of nine patients. In four cases both pathogens were isolated. **CONCLUSIONS:** SARS is a condition associated with substantial morbidity and mortality. It appears to be of viral origin, with patterns suggesting droplet or contact transmission. The role of human metapneumovirus, a novel coronavirus, or both requires further investigation. [Notice: Because of possible public health implications, this article has been published at www.nejm.org on March 31, 2003.]

N Engl J Med 2003 Apr 4; [epub ahead of print]

Spectrum of clinical illness in hospitalized patients with "common cold" virus infections.

The viruses associated most frequently with the "common cold" are rhinoviruses and coronaviruses. The first prospective cohort study to determine the prevalence of rhinovirus and coronavirus infections in patients of all ages hospitalized for acute respiratory illnesses is described. Hospital admissions for acute respiratory illnesses were identified, and cell culture for rhinovirus and serologic assays on paired sera for coronaviruses 229E and OC43 were performed. A total of 61 infections with rhinoviruses and coronaviruses were identified from 1198 respiratory illnesses (5.1%); in addition, nine additional infections associated with ≥ 1 other respiratory viruses were identified. Of those infected with only rhinovirus or coronavirus, underlying cardiopulmonary diseases were present in 35% of the patients aged ≤ 5 years, in 93% aged between five and 35 years, and in 73% aged >35 years. The predominant clinical syndromes varied by age: pneumonia and bronchiolitis in children aged ≤ 5 years; exacerbations of asthma

in older children and young adults; and pneumonia and exacerbations of chronic obstructive pulmonary disease and congestive heart failure in older adults. Therefore, rhinovirus and coronavirus infections in hospitalized patients were associated with lower respiratory tract illnesses in all age groups.

Clin Infect Dis 2000 Jul;31(1):96-100

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