

***Rochalimaea henselae*
infection of humans by
domestic cats**

In order to determine the reservoir and vector(s) for *Rochalimaea henselae*, a causative agent of bacillary angiomatosis (BA) and cat scratch disease, and to estimate the percentage of domestic cats with *R. henselae* bacteremia, the authors conducted a hospital-based survey in the Greater San Francisco Bay Region of Northern California.

The patients surveyed were those with or without human immunodeficiency virus infection, with biopsy-confirmed BA, who also had prolonged exposure to at least one pet cat.

Cultures and laboratory studies were performed on blood drawn from pet cats associated with patients with BA. The *Rochalimaea* species infecting pet cats and fleas and causing the BA lesions in human contacts of these cats was identified by culture, polymerase chain reaction-restriction fragment length polymorphism analysis, and DNA sequencing. The presence of *R. henselae* bacteremia in pet cats was documented, and predictor variables for culture positivity were evaluated.

Four patients who met the survey criteria were identified. The *Rochalimaea* species causing BA lesions in these patients was determined to be *R. henselae*. The seven pet cats were found to be bacteremic with *R. henselae*. This bacterium was also detected in fleas taken from an infected cat.

The researchers documented that the domestic cat serves as a major persistent reservoir for *R.*

henselae, with prolonged, asymptomatic bacteremia from which humans, especially the immunocompromised, may acquire potentially serious infections. Antibiotic treatment of infected cats and control of flea infestation are potential strategies for decreasing human exposure to *R. henselae*.

Koehler JE, Glaser CA, Tappero JW: *Rochalimaea henselae* infection: A new zoonosis with the domestic cat as reservoir. *JAMA* 1994;271:531-535.

**Association of chronic
sinusitis with allergy,
asthma, and eosinophilia**

The association between sinus disease and asthma is generally accepted, although the mechanisms involved are not completely understood.

This study evaluated, in patients with chronic sinusitis who were scheduled for sinus surgery, the interrelationships and correlation among the extent of sinus disease, asthma, allergy, culture results, peripheral eosinophilia, and tissue eosinophilia.

The researchers evaluated the patients' computed tomographic scans, serum samples, peripheral blood samples, and surgical biopsy specimens. Extensive disease was present in 30% of the subjects and correlated well with asthma, specific IgE antibodies, and eosinophilia, but not with elevated total IgE. Among patients with peripheral eosinophilia, 87% had extensive disease. All cultures grew aerobic bacteria; anaerobes and fungi were uncommon.

With the use of computed tomo-

graphic scans of patients with chronic sinusitis, the researchers developed a system for quantitating the extent of the disease.

The well-accepted associations of chronic sinusitis with asthma and allergy appear to be restricted to the group with extensive disease. The presence of peripheral eosinophilia in patients with sinusitis indicates a high likelihood of extensive disease.

Newman LJ, Platts-Mills TAE, Phillips CD, et al: Chronic sinusitis: Relationship of computed tomographic findings to allergy, asthma, and eosinophilia. *JAMA* 1994;271:363-367.

**Alzheimer's disease and
general anesthesia**

An association between prior general anesthetic exposure and Alzheimer's disease (AD) has been hypothesized, but no positive link has been found. Nevertheless, repeated exposure and cumulative total of exposure to neurotoxic factors, such as anesthetics, may accelerate the cognitive decline seen in elderly patients.

This population-based, case-control study was conducted to evaluate prior exposure to general anesthesia as a potential risk factor for AD. Incident cases of AD in the Olmsted County, Minnesota, population from 1975 to 1984 were compared with control subjects matched for age and gender, selected from all registrations for care at Mayo Clinic.

The case and control groups each had 252 individuals. Of these, 208 cases and 199 control subjects had at least one exposure to gen-

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Lorcet® 10/650

Each tablet contains: 10 mg hydrocodone bitartrate
(Warning: May be habit-forming) and 650 mg acetaminophen.

Reference:

1. Data on file, Forest Laboratories, New York, NY.

INDICATIONS AND USAGE:

For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS:

Hypersensitivity to acetaminophen or hydrocodone.

WARNINGS: Respiratory Depression:

At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing.

Head Injury and Increased Intracranial Pressure:

The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a preexisting increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions:

The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

PRECAUTIONS: Special Risk Patients:

As with any narcotic analgesic agent, Lorcet® 10/650 should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

Cough Reflex:

Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when Lorcet® 10/650 is used postoperatively and in patients with pulmonary disease.

Drug Interactions:

Patients receiving other narcotic analgesics, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with Lorcet® 10/650 may exhibit an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced. The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone. The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus.

Usage in Pregnancy:

Teratogenic Effects: Pregnancy Category C. Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. Lorcet® 10/650 should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects:

Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose. There is no consensus on the best method of managing withdrawal. Chlorpromazine 0.7 to 1 mg/kg q6h, and paregoric 2 to 4 drops/kg q4h, have been used to treat withdrawal symptoms in infants. The duration of therapy is 4 to 28 days, with the dosage decreased as tolerated.

Labor and Delivery:

As with all narcotics, administration of Lorcet® 10/650 to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

Nursing Mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Lorcet® 10/650, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

Safety and effectiveness in children have not been established. The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include: **Central Nervous System:** Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence, mood changes. **Gastrointestinal System:** The antiemetic phenothiazines are useful in suppressing the nausea and vomiting which may occur (see above); however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia. Prolonged administration of Lorcet® 10/650 may produce constipation. **Genitourinary System:** Ureteral spasm, spasm of vesical sphincters and urinary retention have been reported. **Respiratory Depression:** Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. Apply other supportive measures when indicated. **DRUG ABUSE AND DEPENDENCE:** Lorcet® 10/650 is subject to the Federal Controlled Substances Act (Schedule III). Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, Lorcet® 10/650 should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when Lorcet® 10/650 is used for a short time for the treatment of pain. **OVERDOSAGE: Acetaminophen:** Signs and Symptoms: In acute acetaminophen overdose, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion. **Hydrocodone:** Signs and Symptoms: Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur. **DOSAGE AND ADMINISTRATION:** Dosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related. The usual adult dosage is one tablet every four to six hours as needed for pain. The total 24 hour dose should not exceed 6 tablets. **CAUTION:** Federal law prohibits dispensing without prescription. A Schedule III Controlled Substance. Manufactured by: **MIKART, INC.** ATLANTA, GA 30318 Manufactured for **UAD Laboratories Division of Forest Pharmaceuticals, Inc.** Jackson, MS 39209 Rev. 11/92 Code 558A00

medi-notes

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eral anesthesia prior to the year of onset of dementia in the matched AD patient.

The cumulative duration of anesthesia and the total number of general anesthetic exposures prior to the age of onset of dementia and the corresponding year in each matched control subject was ascertained.

The results of the study show no significant difference in mean cumulative exposure (in minutes) to general anesthesia (patients vs control individuals: 188.4 vs 170.5 minutes, not significant). Neither exposure to six or more episodes of general anesthesia nor cumulative exposure to 600 minutes or more of general anesthesia was associated with a significantly increased risk of AD.

The authors concluded that multiple exposures to general anesthesia are not likely to increase the risk of AD.

Bohnen NILJ, Warner MA, Kokmen E, et al: Alzheimer's disease and cumulative exposure to anesthesia: A case-control study *J Am Geriatr Soc* 1994;42:198-201.

Noninvasive detection of malignancy by identification of unusual CD44 gene activity in exfoliated cancer cells

The authors report on the results of their investigation of noninvasive cancer detection by testing for unusual CD44 gene activity in a clinical sample as an indicator of exfoliated tumor cells.

Forty-four unselected, consecutive patients with bladder cancer and 46 people with no evidence

of neoplasia participated in the investigation.

Novel abnormalities in the pattern of expression of CD44 gene, seen specifically in tumor tissue, led to cloning of a newly recognized coding region in it (exon 6). This was tested as a probe for detection of exfoliated malignant cells in naturally voided urine. CD44 gene products extracted from the urine and amplified with polymerase chain reaction contained predicted electrophoretic band of 735 base pairs in 40 of the 44 patients with bladder cancer. Products from 38 of the 46 people with no evidence of neoplasia showed no such band.

The investigation confirmed the unusual activity of the CD44 locus in the neoplasia and the malignancy. Techniques for the analysis of such activity can enable noninvasive investigation of patients for primary or recurrent bladder cancer or for other tumors that shed neoplastic cells into body fluids.

Matsumura Y, Hanbury D, Smith J, et al: Non-invasive detection of malignancy by identification of unusual CD44 gene activity in exfoliated cancer cells. *BMJ* 1994; 308:619-624.

Are seasonal variations in plasma fibrinogen and FVIIc linked to excess CVD-related winter deaths?

Approximately 20,000 more deaths from cardiovascular disease (CVD) occur in England and Wales during an average winter than during other times of the year. The reasons for the excess have not been fully elucidated.

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