

Ultrasound Aids Pediatric Appendicitis Diagnosis

A new classification eases surgical decision making by elevating the importance of secondary signs.

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — A new ultrasound classification facilitates surgical decision making in the diagnosis or exclusion of appendicitis in children by elevating the importance of secondary signs, according to a study presented at the annual meeting of the Radiological Society of North America. “This ultrasound classification improves sensitivity in children with suspected acute appendicitis. The presence of secondary signs makes acute appendicitis most likely, and the absence of these signs can safely rule out acute appendicitis in children,” said Dr. Fraukje Wiersma.

This evaluation of a new classification for diagnosing pediatric appendicitis

comes at a time of increasing concern over the widespread use of computed tomography (CT) and the radiation risk it poses to children.

“Furthermore, the lack of abdominal fat in children makes them less suitable for CT,” said Dr. Wiersma, of The Hague (the Netherlands) Medical Center.

‘This classification ... prevents a high rate of negative appendectomies and [also prevents] complications of unrecognized appendicitis.’

In the standing literature, the abdominal ultrasound is considered positive only when an inflamed appendix is depicted by the sonogram.

“Although secondary signs such as inflamed fat or fluid are described, they are considered to be nonspecific findings and are excluded in the calculation of sensitivity, specificity, and predictive values,” Dr. Wiersma said in an interview.

Between May 2005 and June 2006, Dr. Wiersma and her colleagues conducted ultrasound examinations of 212 consecutive

pediatric patients aged 2-15 years with suspected appendicitis. Their mean age was 10 years, and 129 of the children were boys.

Depiction of the appendix was classified into four groups: in group 1, the appendix was normal; in group 2, the appendix was not depicted and no secondary signs of appendicitis were present; in group 3, the appendix was not depicted, but secondary signs of appendicitis (inflamed fat or fluid) were present; in group 4, an inflamed appendix was depicted. Patients in the first two groups had negative ultrasounds for appendicitis, whereas those in the latter two groups were considered positive and were treated surgically, she explained.

Ultrasonographic diagnoses were correlated with histopathological results or clinical follow-up. In addition, the investigators calculated the negative appendectomy rate, the perforation rate, and predictive values of this four-part classification scheme.

Among the 96 patients in group 1, there was one false-negative, a patient who subsequently developed acute appendicitis.

Among the 41 patients in group 2 (those with no secondary signs), none had acute appendicitis at follow-up.

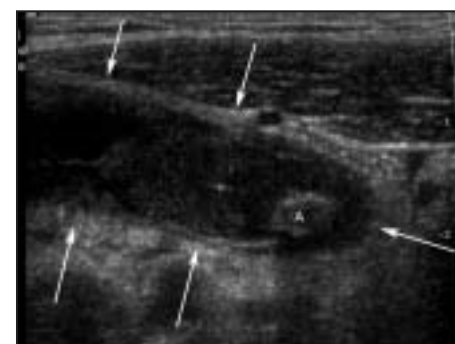
In group 3 (those with secondary signs, including local dilated small-bowel loop, local fluid collections, and/or increased echogenicity of mesenteric fat), 8 of the 10 patients had acute appendicitis, whereas 2 patients had negative appendectomies (1 had primary peritonitis and the other had a necrotic lymph node resected).

Of the 65 patients in group 4 in whom ultrasound had detected an inflamed appendix, 62 had acute appendicitis. Of the remainder, one patient had chronic inflammatory signs on pathological evaluation, one had a negative appendectomy (a true false-positive), and one was not operated on because of a “miscommunication” and left the hospital without further complaint.

“The prevalence of acute appendicitis in this study population was 34%, and the negative appendix read rate was comparable to that of other ultrasonograph-



This ultrasound image shows a transverse section of a normal appendix with compression (white arrows).



This ultrasound image shows a longitudinal section of an inflamed appendix (white arrows) with increased echogenicity of mesenteric fat (A = appendicolith).

PHOTOS COURTESY DR. FRAUKJE WIERSMA

ic and CT studies,” Dr. Wiersma said. The classification developed by these Dutch researchers, under the direction of Dr. Herma C. Holscher, had a sensitivity of 99%, a specificity of 96%, a positive predictive value of 93%, a negative predictive value of 99%, and an accuracy of 97%, she reported.

Dr. Wiersma added that the sensitivity—but not specificity—is significantly higher than that of the standard method (87%) described in the literature, when applied to this study population.

“This classification of the ultrasonographic depiction of the appendix and surrounding area has high predictive values in children with suspected appendicitis, and prevents a high rate of negative appendectomies and complications of unrecognized appendicitis,” Dr. Wiersma concluded.

Gris-PEG[®] (griseofulvin ultramicronized) Tablets, USP 125 mg; 250 mg

DESCRIPTION
Gris-PEG[®] Tablets contain ultramicronized crystals of griseofulvin, an antibiotic derived from a species of *Penicillium*. Each Gris-PEG tablet contains:
Active Ingredient: griseofulvin ultramicronized ... 125 mg
Inactive Ingredients: colloidal silicon dioxide, lactose, magnesium stearate, methylcellulose, methylparaben, polyethylene glycol 400 and 8000, povidone, and titanium dioxide.
OR
Active Ingredient: griseofulvin ultramicronized ... 250 mg
Inactive Ingredients: colloidal silicon dioxide, magnesium stearate, methylcellulose, methylparaben, polyethylene glycol 400 and 8000, povidone, sodium lauryl sulfate, and titanium dioxide.

ACTION
Microbiology—Griseofulvin is fungistatic with *in vitro* activity against various species of *Microsporum*, *Epidermophyton* and *Trichophyton*. It has no effect on bacteria or other genera of fungi.
Pharmacokinetics—Following oral administration, griseofulvin is deposited in the keratin precursor cells and has a greater affinity for diseased tissue. The drug is tightly bound to the new keratin which becomes highly resistant to fungal invasions.
The efficiency of gastrointestinal absorption of ultramicronized griseofulvin is approximately one and one-half times that of the conventional microsize griseofulvin. This factor permits the oral intake of two-thirds as much ultramicronized griseofulvin as the microsize form. However, there is currently no evidence that this lower dose confers any significant clinical differences with regard to safety and/or efficacy. In a bioequivalence study conducted in healthy volunteers (N=24) in the fasted state, 250 mg ultramicronized griseofulvin tablets were compared with 250 mg ultramicronized griseofulvin tablets that were physically altered (crushed) and administered with applesauce. The 250 mg ultramicronized griseofulvin tablets were found to be bioequivalent to the physically altered (crushed) 250 mg ultramicronized griseofulvin tablets (See Table 1).

Table 1: Mean (± SD) of the Pharmacokinetic Parameters for Griseofulvin administered in applesauce as a Single Dose of Gris-PEG[®] 250-mg Tablets Uncrushed and Crushed to Fasted Healthy Volunteers (N=24)

| | 250 mg Ultramicronized Griseofulvin Tablets Unaltered | 250 mg Ultramicronized Griseofulvin Tablets Physically Altered (Crushed and in Applesauce) |
|--------------------------|---|--|
| C _{max} (ng/mL) | 600.61 (± 167.6) | 672.61 (± 146.2) |
| T _{max} (hr) | 4.04 (± 2.2) | 3.08 (± 1.02) |
| AUC (ng·hr/mL) | 8618.89 (± 1907.2) | 9023.71 (± 1911.5) |

INDICATIONS
Gris-PEG (griseofulvin ultramicronized) is indicated for the treatment of the following ringworm infections: tinea corporis (ringworm of the body), tinea pedis (athlete’s foot), tinea cruris (ringworm of the groin and thigh), tinea barbae (barber’s itch), tinea capitis (ringworm of the scalp), and tinea unguium (onychomycosis, ringworm of the nails), when caused by one or more of the following genera of fungi: *Trichophyton rubrum*, *Trichophyton tonsurans*, *Trichophyton mentagrophytes*, *Trichophyton interdigitale*, *Trichophyton verrucosum*, *Trichophyton megnini*, *Trichophyton gallinae*, *Trichophyton crateriform*, *Trichophyton sulphureum*, *Trichophyton schoenleinii*, *Microsporum audouinii*, *Microsporum canis*, *Microsporum gypseum*, and *Epidermophyton floccosum*. NOTE: Prior to therapy, the type of fungi responsible for the infection should be identified. The use of the drug is not justified in minor or trivial infections which will respond to topical agents alone. Griseofulvin is not effective in the following: bacterial infections, candidiasis (moniliasis), histoplasmosis, actinomycosis, sporotrichosis, chromoblastomycosis, coccidioidomycosis, North American blastomycosis, cryptococcosis (torulosis), tinea versicolor and nocardiosis.

CONTRAINDICATIONS
Two cases of conjoined twins have been reported since 1977 in patients taking griseofulvin during the first trimester of pregnancy. Griseofulvin should not be prescribed to pregnant patients. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. This drug is contraindicated in patients with porphyria or hepatocellular failure and in individuals with a history of hypersensitivity to griseofulvin.

WARNINGS
Prophylactic Usage—Safety and efficacy of griseofulvin for prophylaxis of fungal infections have not been established.
Animal Toxicology—Chronic feeding of griseofulvin, at levels ranging from 0.5%-2.5% of the diet resulted in the development of liver tumors in several strains of mice, particularly in males. Smaller particle sizes result in an enhanced effect. Lower oral dosage levels have not been tested. Subcutaneous administration of relatively small doses of griseofulvin once a week during the first three weeks of life has also been reported to induce hepatomas in mice. Thyroid tumors, mostly adenomas but some carcinomas, have been reported in male rats receiving griseofulvin at levels of 2.0%, 1.0% and 0.2% of the diet, and in female rats receiving the two higher dose levels. Although studies in other animal species have not yielded evidence of tumorigenicity, these studies were not of adequate design to form a basis for conclusion in this regard. In subacute toxicity studies, orally administered griseofulvin produced hepatocellular necrosis in mice, but this has not been seen in other species. Disturbances in porphyrin metabolism have been reported in griseofulvin-treated laboratory animals. Griseofulvin has been reported to have a colchicine-like effect on mitosis and cocarcinogenicity with methylnanthrene in cutaneous tumor induction in laboratory animals.

PRECAUTIONS
Pregnancy—See CONTRAINDICATIONS section.
Animal Reproduction Studies—It has been reported in the literature that griseofulvin was found to be embryotoxic and teratogenic on oral administration to pregnant rats. Pups with abnormalities have been reported in the litters of a few bitches treated with griseofulvin. Suppression of spermatogenesis has been reported to occur in rats, but investigation in man failed to confirm this.

ADVERSE REACTIONS
When adverse reactions occur, they are most commonly of the hypersensitivity type such as skin rashes, urticaria, erythema multiforme-like drug reactions, and rarely, angioneurotic edema, and may necessitate withdrawal of therapy and appropriate countermeasures. Paresthesia of the hands and feet have been reported rarely after extended therapy. Other side effects reported occasionally are oral thrush, nausea, vomiting, epigastric distress, diarrhea, headache, fatigue, dizziness, insomnia, and impairment of performance of routine activities. Proteinuria and leukopenia have been reported rarely. Administration of the drug should be discontinued if granulocytopenia occurs. When rare, serious reactions occur with griseofulvin, they are usually associated with high dosages, long periods of therapy, or both.

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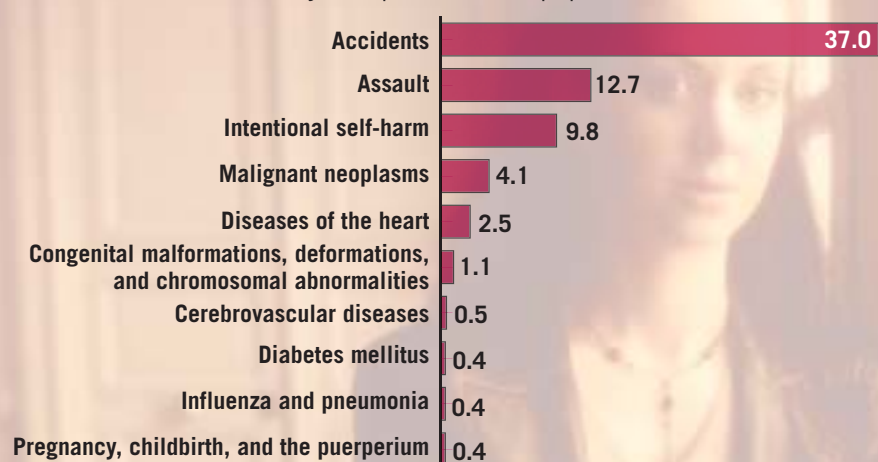
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DATA WATCH

Top 10 Causes of Death for People Aged 15-24 Years
(mortality rate per 100,000 population)



Source: 2005 preliminary data, Centers for Disease Control and Prevention

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