

# The Early Diagnosis of *Campylobacter* Enteritis by Wet-Mount Examination

Brian J. Murray, MD  
La Jolla, California

*Campylobacter* enteritis is now recognized as the most common acute bacterial diarrheal illness in man.<sup>1-4</sup> At the University of California, San Diego, Student Health Center, *Campylobacter fetus* subspecies *jejuni* has accounted for 25 percent of all cases of acute diarrheal illness and 90 percent of all cases of acute bacterial enteritis.<sup>5</sup> Obviously a presumptive diagnosis of *Campylobacter* enteritis determined by a test available in the office using a simple microscopic examination of an unstained wet-mount stool specimen would be highly desirable. In addition, knowing which stools to culture, based on microscopic examination, would be advantageous.

It is known that dark-field microscopy, phase-contrast microscopy, or a Gram stain of a stool specimen can sometimes permit a rapid diagnosis of *Campylobacter* enteritis by identification of the organism or its motility.<sup>6-8</sup> Others have shown a significant correlation of fecal leukocytes, seen with methylene blue stain, for *Shigella* or *Salmonella* enteritis.<sup>9,10</sup> It is thought that *Campylobacter* enteritis, presenting as an inflammatory diarrhea, should demonstrate fecal leukocytes as well.

This prospective study was done to assess the value of using an unstained, wet-mount stool specimen examination for making either a presumptive or predictive diagnosis of *Campylobacter* enteritis. In addition, this study was done to determine whether the results of the wet-mount stool examination can serve as a guide for determining which stools should be cultured.

## Methods

During a recent eight-month period all stool specimens from patients with acute diarrheal illness were studied. All patients, 95 percent of whom were aged 18 to 25 years, were enrolled at the University of California, San Diego, and seen at the Student Health Center. Diarrhea defined as acute was of less than ten days' duration, with stools of watery, loose consistency, and with a frequency of at least twice normal.

Fresh stool specimens were submitted and evaluated within one-half hour; no rectal swabs were used. A wet-mount examination was prepared using one drop of tryptic soy broth mixed with a portion of the liquid stool on a glass slide. The field was scanned for leukocytes, erythrocytes, ova and parasites, and darting organisms, whose typical appearance is well-described elsewhere.<sup>6,7</sup> The degree of fecal leukocytosis was graded as heavy, greater than 15 white blood cells (WBC) per high power field (HPF); moderate, 5 to 15 WBC/HPF; few, 1 to 5 WBC/HPF; and rare, less than 1 WBC/HPF. A Hemocult test was performed on all specimens. If fecal leukocytes or erythrocytes were seen or if a Hemocult card was positive, the stool was cultured. Stool specimens were randomly cultured from ten patients with acute diarrhea who did not exhibit any fecal leukocytes or erythrocytes or have a positive Hemocult test.

Stool specimens for isolating *Campylobacter fetus* subspecies *jejuni* were inoculated onto a selective plating medium of Campy-BAP and incubated at 42°C in a *Campylobacter* environment-chamber gas-generating kit. After incubation of

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**Azo Gantrisin®**  
Each tablet contains 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl.

Before prescribing, please consult complete product information, a summary of which follows:

**INDICATIONS:** Initial treatment of uncomplicated urinary tract infections caused by susceptible strains of *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Proteus mirabilis*, *Proteus vulgaris* and *Staphylococcus aureus* when relief of pain, burning or urgency is needed during first 2 days of therapy. Azo Gantrisin treatment not to exceed 2 days. Evidence lacking that sulfisoxazole plus phenazopyridine HCl better than sulfisoxazole alone after 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche). (See DOSAGE AND ADMINISTRATION.) **Important Note:** Coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. With ongoing therapy, add aminobenzoic acid to culture media. Increasing resistance of organisms may limit sulfonamide usefulness. As identical doses produce wide variations, measure blood levels in patients receiving sulfonamides for serious infections: 12 to 15 mg/100 ml is optimal; adverse reactions are more frequent above 20 mg/100 ml.

**CONTRAINDICATIONS:** Children under 12; known sensitivity to either component; pregnancy at term and during nursing period; in glomerulonephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

**WARNINGS:** Sulfonamides are bacteriostatic; organisms causing common infections are often resistant. Sulfas won't eradicate group A streptococci or prevent sequelae like rheumatic fever and glomerulonephritis. Deaths from hypersensitivity reactions, hepatocellular necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Perform blood counts and renal function tests.

**PRECAUTIONS: General:** Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma. Hemolysis may occur in glucose-6-phosphate dehydrogenase-deficient individuals.

The more soluble sulfonamides are associated with fewer renal complications. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Information for Patients:** Maintain adequate fluid intake; urine will turn reddish-orange.

**Laboratory Tests:** Perform urinalysis with careful microscopic examination at least once a week and regular blood counts after 2 weeks therapy; measure blood levels in patients with serious infection (see INDICATIONS). **Drug Interactions:** Sulfonamides may displace oral anticoagulants from plasma protein binding sites, increasing anticoagulant effect. Can also displace methotrexate. **Drug Laboratory Test Interactions:** May affect liver function tests in hepatitis.

**Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis:** Azo Gantrisin has not undergone adequate trials relating to carcinogenicity; each component, however, has been evaluated separately. Rats appear especially susceptible to goitrogenic effects of sulfonamides; long-term administration has resulted in thyroid malignancies in this species. Long-term administration of phenazopyridine HCl has induced neoplasia in rats (large intestine) and mice (liver). No association between phenazopyridine HCl and human neoplasia reported; adequate epidemiological studies have not been conducted. **Mutagenesis:** No studies available. **Impairment of Fertility:** The components of Azo Gantrisin have been evaluated in animal reproduction studies. In rats given 800 mg/kg/day sulfisoxazole, there were no effects on mating behavior, conception rate or fertility index. Fertility was not affected in a two-litter study of rats given 50 mg/kg/day phenazopyridine.

**Pregnancy: Teratogenic Effects:** Pregnancy Category C. The components of Azo Gantrisin have been evaluated. At 800 mg/kg/day sulfisoxazole was nonteratogenic in rats and rabbits, with no perinatal or postnatal effects in rats. In two other studies, cleft palates developed in rats and mice after 500 to 1000 mg/kg/day sulfisoxazole. No congenital malformations developed in rats given 50 mg/kg/day phenazopyridine. As there are no satisfactory animal or human studies, it is not known whether Azo Gantrisin can cause fetal harm or affect reproduction capacity. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nonteratogenic Effects, Nursing Mothers and Pediatric Use:** See CONTRAINDICATIONS.

**ADVERSE REACTIONS: Allergic:** Anaphylaxis, generalized allergic reactions, angioneurotic edema, arteritis and vasculitis, myocarditis, serum sickness, conjunctival and scleral injection, periarthritis nodosa, systemic lupus erythematosus. **Cardiovascular:** Tachycardia, palpitations, syncope, cyanosis. **Dermatologic:** Rash, urticaria, pruritus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, photosensitivity. **Endocrine:** Goiter production, diuresis, hypoglycemia. Cross-sensitivity with some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents may exist. **Gastrointestinal:** Nausea, emesis, abdominal pain, anorexia, diarrhea, glossitis, stomatitis, flatulence, salivary gland enlargement, G.I. hemorrhage, pseudomembranous enterocolitis, meliaria, pancreatitis, hepatic dysfunction, jaundice, hepatocellular necrosis. **Genitourinary:** Crystalluria, hematuria, BUN and creatinine elevation, nephritis and toxic nephrosis with oliguria and anuria, acute renal failure, urinary retention. **Hematologic:** Leukopenia, agranulocytosis, aplastic anemia, thrombocytopenia, purpura, hemolytic anemia, anemia, eosinophilia, clotting disorders including hypoprothrombinemia and hypofibrinogenemia, sulfhemoglobinemia, methemoglobinemia. **Musculoskeletal:** Arthralgia, chest pain, myalgia. **Neurologic:** Headache, dizziness, peripheral neuritis, paresthesia, convulsions, tinnitus, vertigo, ataxia, intracranial hypertension. **Psychiatric:** Psychosis, hallucinations, disorientation, depression, anxiety. **Miscellaneous:** Edema (including periorbital), pyrexia, drowsiness, weakness, fatigue, lassitude, rigors, flushing, hearing loss, insomnia, pneumonitis.

**OVERDOSAGE: Signs:** Anorexia, colic, nausea, vomiting, dizziness, drowsiness, unconsciousness; possibly pyrexia, hematuria, crystalluria. Blood dyscrasias and jaundice may occur later. **Treatment:** Institute gastric lavage or emesis; force oral fluids; administer intravenous fluids if urine output is low with normal renal function. Monitor blood counts and appropriate blood chemistries, including electrolytes. In cyanosis, consider methemoglobinemia and treat with intravenous 1% methylene blue. Institute specific therapy for blood dyscrasias or jaundice.

**DOSAGE AND ADMINISTRATION:** Azo Gantrisin is intended for the acute, painful phase of urinary tract infections. The recommended dosage in adults is 4 to 6 tablets initially, followed by 2 tablets four times daily for up to 2 days. Treatment with Azo Gantrisin should not exceed 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche).

**HOW SUPPLIED:** Tablets, each containing 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl—bottles of 100 and 500.

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the culture, the colonies were readily identified by their typical Gram stain, motility, and biochemical properties.<sup>3,11</sup> Confirmation of each positive *Campylobacter* culture was made by sending a subculture to the local public health department. The decision not to culture stool specimens with negative microscopic findings was based on previous experience and that of others.<sup>3,5,12</sup>

## Results

A total of 267 specimens were evaluated, and 173 revealed some degree of fecal leukocytosis, red cells, or a positive Hemocult; 166 revealed some degree of fecal leukocytosis. Of the 173 specimens plated for culture, 64 had *Campylobacter fetus* subspecies *jejuni* found on culture and 9 had either a *Salmonella* or a *Shigella* species isolate. All specimens with positive *Campylobacter* cultures had some degree of fecal leukocytes on the wet-mount examination. Only 50 percent of cultures for *Campylobacter* had a positive Hemocult test, and 81 percent had erythrocytes seen on the wet-mount examination.

When wet-mount examination revealed a moderate or heavy range of fecal leukocytes, *Campylobacter fetus* subspecies *jejuni* was identified on culture in 55 percent. Finding five or more fecal leukocytes on the wet-mount examination revealed a 89 percent sensitivity and a 51 percent specificity for the early diagnosis of *Campylobacter enteritis* (Table 1). Darting organisms were seen in 32 percent (21/64) of all cases of *Campylobacter enteritis*. Finding darting organisms in the fecal smear was pathognomonic for *Campylobacter enteritis* with a 100 percent predictive value. The ten control stool specimens cultured from patients with acute diarrhea and negative microscopic findings all had no growth for bacterial pathogens.

## Comment

This study confirms the value of performing a screening wet-mount examination on stool specimens of patients with acute diarrhea. In nearly one third of all cases of *Campylobacter enteritis*,



Table 1. Results of the Wet-Mount Examination for Fecal Leukocytes and Stool Cultures (n)			
Fecal Leukocytes per HPF	Stool Culture Results		
	Campylobacter Positive	Campylobacter Negative	Salmonella or Shigella Positive
≥ 5 (n=112)	57	46	9
> 0 and < 5 (n=54)	7	47	0

darting organisms were seen on wet-mount examination. This finding has had 100 percent specificity for the presumptive diagnosis of Campylobacter enteritis. This study also shows that if fecal leukocytes are not seen on the wet-mount stool examination, the yield for a positive stool culture for Campylobacter is negligible, and with fewer than 5 WBC/HPF the diagnostic yield is low. On the other hand, when five or more fecal leukocytes are seen on the wet-mount examination, there has been an 89 percent sensitivity for identifying Campylobacter enteritis. Hemocult testing and stool smear examination for erythrocytes were not so helpful in making a predictive diagnosis for Campylobacter enteritis.

Dark-field or phase-contrast microscopy of a stool specimen to identify the Campylobacter organism is not practical in the general primary care practice. Rather, a simple, quick, reliable method for making an early diagnosis of Campylobacter enteritis using light microscopy on an unstained, wet-mount stool specimen is highly favored. This study shows it is not necessary to stain a stool specimen slide to identify fecal leukocytes or darting organisms.

The wet-mount examination can serve as a guide to determine which stool specimens merit culturing. If any fecal leukocytes are seen on the wet-mount examination, the specimen should be cultured. At this health center finding five or more white blood cells per high-power field on the stool wet-mount has had a strong predictive value for bacterial enteritis, which is primarily due to Campylobacter. Furthermore, in one third of all cases of Campylobacter enteritis, the wet-mount

examination has led to an immediate and accurate diagnosis. The use of this simple, inexpensive examination should be done routinely on all patients with acute diarrhea.

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