



The reader is encouraged to write possible diagnoses for each case before turning to the discussion. We invite readers to contribute case presentations and discussions. Please inquire first by contacting Dr. Nazarian at LFredN@aol.com.

Author Disclosure

Drs Tamma, Migeon, Ghosh, Loddenkemper, Wright, Phillips, Levien, Prayson, Hashkes, and Dixon did not disclose any financial relationships relevant to this article.

To view *Suggested Reading lists* for these cases, visit www.pedsinreview.org and click on *Index of Suspicion*

Frequently Used Abbreviations

ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
BUN:	blood urea nitrogen
CBC:	complete blood count
CNS:	central nervous system
CSF:	cerebrospinal fluid
CT:	computed tomography
ECG:	electrocardiography
ED:	emergency department
EEG:	electroencephalography
ESR:	erythrocyte sedimentation rate
GI:	gastrointestinal
GU:	genitourinary
Hct:	hematocrit
Hgb:	hemoglobin
MRI:	magnetic resonance imaging
WBC:	white blood cell

Case 1 Presentation

A 16-year-old Caucasian girl comes in for a health supervision visit. She has been in good health, although she is concerned that she has not achieved menarche. Both her mother and sister attained menarche at age 13 years. She denies any unusual dieting patterns and has not been sexually active.

On physical examination, she is a pleasant girl whose height is far above the 97th percentile, weight is at the 10th percentile, and body mass index is 14.8. Her thyroid gland is not palpable. Her breasts are at Sexual Maturity Rating 3. She has normal abdominal findings when examined supine, but when standing and coughing, a 3.5-cm mass is palpable in her left inguinal canal. Her external genitalia have a normal female appearance, without clitoromegaly. She has minimal coarse pubic hair and no facial or axillary hair. The remainder of her physical findings are normal. Further testing reveals the reason for her delayed menarche.

Case 2 Presentation

A 16-year-old boy has a 2-month history of progressive, reddish-purple, nonpainful, nonpruritic swelling around both eyes. There have been no other systemic features, including other rashes, joint pain, or muscle weakness. Orbital CT shows only periorbital soft-tissue swelling. Skin testing shows 3+ reactions to dust mite, dog, guinea pig, trees, grass, and weeds. He has not responded to oral steroids, intraleSIONAL steroid injections, or multiple antibiotics. Other than his ocular findings, the only positive physical findings include left sternocleidomastoid atrophy and minimal neck weakness.

He has a WBC count of $3.86 \times 10^3/\text{mcL}$ ($3.86 \times 10^9/\text{L}$) with

lymphopenia and thrombocytopenia ($125 \times 10^3/\text{mcL}$ [$125 \times 10^9/\text{L}$]). Bone marrow biopsy shows mild hypocellularity without signs of malignancy. The ESR and C-reactive protein, serum immunoglobulin, and complement levels are normal. Enzyme levels include AST of 47 U/L (normal, <40 U/L), lactate dehydrogenase (LDH) of 362 U/L (normal, <220 U/L), creatine kinase (CK) of 123 U/L (normal, <192 U/L); CK myocardial band fraction (CK-MB) of 19.1 ng/mL (normal, <8.8 ng/mL), and aldolase of 12.1 U/L (normal, <8 U/L).

He has normal thyroid and renal profiles. von Willebrand antigen activity is 192% (normal, $<145\%$). Repeated blood cultures and serologic tests for *Mycoplasma*, fungal, and Epstein-Barr infection are negative. Antinuclear, extractable nuclear (RNP, SS-A, SS-B, Sm), Jo-1, histone, Scl-70 centromere, antiplatelet, antineutrophil, and antineutrophil cytoplasmic antibodies are negative. CT scans of the neck, chest, and abdomen show normal findings except for atrophy of the left sternocleidomastoid muscle. MRI of the brain and orbit and MR angiography show only preseptal swelling.

Case 3 Presentation

A 16-year-old girl comes to the ED because of shortness of breath and chest pain. Her symptoms began with fever and chills 4 days ago; vomiting and dyspnea started yesterday.

On physical examination, although awake and alert, the girl is uncomfortable and unable to speak in complete sentences because of the shortness of breath. She complains of chest pain with inspiration. Her respiratory rate is 42 breaths/min, and her pulse oximetry saturation is 90% in room air. Her temperature is 101.2°F (38.5°C), heart rate is

83 beats/min, and blood pressure is 130/77 mm Hg. She has intercostal retractions and shallow respirations. Decreased breath sounds and dullness to percussion are noted at both lung bases. The remainder of her physical findings are normal.

Initial laboratory studies reveal a WBC count of $22.9 \times 10^3/\text{mCL}$ ($22.9 \times 10^9/\text{L}$), (80% neutrophils, 12% bands, 6% lymphocytes, 2% monocytes), Hgb concentration of 11.1 g/dL (111 g/L), and platelet count of $313 \times 10^3/\text{mCL}$ ($313 \times 10^9/\text{L}$). Her serum sodium concentration is 133 mEq/L (133 mmol/L). All other electrolyte concentrations are within normal limits. A chest radiograph taken in the ED shows bilateral infiltrates with small, bilateral pleural effusions. There is no evidence of pneumothorax or pneumomediastinum.

She is admitted and given oxygen by nasal cannula in addition to intravenous ceftriaxone. Later that day, her respiratory distress worsens, and she is transferred to the pediatric intensive care unit.

Case 1 Discussion

In this patient, the main concern was primary amenorrhea. A pelvic examination revealed absence of a uterus. Chromosomal analysis revealed a 46,XY karyotype. Androgen insensitivity was suspected, and hormone testing was performed. The girl's follicle-stimulating hormone (FSH) level was 1.4 mIU/mL (1.4 IU/L) (normal male range, 1.4 to 18.1 mIU/mL [1.4 to 18.1 IU/L]). Her luteinizing hormone (LH) level was 35 mIU/mL (normal male range, 1.5 to 9.3 mIU/mL), and her testosterone level was 1,088 ng/dL (37.8 nmol/L) (normal range, 241 to 827 ng/dL [8.4 to 28.7 nmol/L]). A low FSH level and high levels of LH and testosterone

are consistent with androgen insensitivity. Complete androgen insensitivity syndrome (CAIS) was diagnosed. Pelvic ultrasonography was performed to locate the testes.

The Condition

In 1950, Wilkins described a 30-year-old patient who was phenotypically female but lacked pubic and axillary hair. (1) She was interested in growing body hair, but despite the local application of testosterone, there was neither growth of sexual hair nor any other androgenic effects. Wilkins concluded that her syndrome was related to an "insensitivity of end organs to androgen." Since that time, androgen insensitivity syndromes have become recognized as clinical entities, with the incidence of CAIS estimated to be as high as 1 in 20,000.

Pathogenesis

Testosterone is the primary androgen synthesized and secreted by the testes. Tissue-specific expression of the enzyme 5-alpha reductase converts testosterone to its active metabolite, dihydrotestosterone (DHT). Within target cells, DHT and, to a lesser extent, testosterone bind to androgen receptors. In CAIS, there is a resistance to androgens due to defects in the androgen receptor. Some patients have no detectable androgen receptors, while others have a near-normal number of androgen receptors but abnormal androgen receptor binding. Less commonly, both the number and the function of the androgen receptor are diminished.

The chromosomal basis of androgen insensitivity is a loss-of-function mutation in the *AR* gene that has been localized to the long arm of the X chromosome and affects all receptors. Although numerous deletions have been described, including complete and partial gene deletions,

more than 80% of patients have a single amino acid substitution.

Clinical Features

In patients who have CAIS, although the labia majora and minora sometimes may appear slightly underdeveloped, the general appearance of the external genitalia is unquestionably female. A clitoris is present always, but never enlarged. Both the urethral and vaginal openings always are in the normal position. Although the length of the vagina may be normal, often it is short. The vagina ends blindly, and neither a cervix nor a uterus can be palpated during a bimanual examination.

Because of the generally normal secretion of müllerian-inhibiting factor by Sertoli cells of the testes, development of the müllerian ducts usually is suppressed. Patients who have CAIS never menstruate because they do not possess a uterus nor can they become pregnant. Due to the absence of scrotal development, the testes are located in the abdomen or at various levels in the inguinal canal, attempting to descend into the labial folds. CAIS should be suspected in phenotypically normal females who have inguinal hernias or labial masses. As many as 1% to 2% of girls who develop inguinal hernias have this disorder.

Despite normal androgen synthesis, typical androgen effects such as acne and voice changes are blunted due to androgen resistance. Patients who have CAIS usually are taller than unaffected women, suggesting that the Y chromosome may have effects not mediated by androgens.

Adolescents afflicted with CAIS have a normal female body habitus, often with well-developed breasts. Testosterone is converted to 17-beta estradiol by aromatase in the adrenal gland, testes, and adipose tissue, providing a source of estrogen that can

bind to estrogenic receptors and promote breast and bone development.

Partial androgen insensitivity syndrome also can occur in individuals who have a 46,XY genotype. Affected patients are born with ambiguous external genitalia due to their partial ability to respond to androgens. The genital tubercle is larger than a clitoris but smaller than a penis. Often, partially fused labia or a scrotum are present. The testes may be undescended, and hypospadias often is present. Wolffian duct development is either minimal or nonexistent, and the müllerian duct system does not develop.

A Similar Condition

Gonadal dysgenesis is another disorder resulting in a female phenotype despite a male genotype. Unlike androgen insensitivity, in which functional testes can produce testosterone, patients born with gonadal dysgenesis have abnormal testes that are incapable of producing androgens. Complete gonadal dysgenesis affects 46,XY individuals and is characterized by abnormally formed gonads that originally were on the path to testis differentiation. External genitalia are female, and there is müllerian duct development and wolffian duct regression. Female external genitalia develop because of the failure of the gonadal streaks to produce androgens to masculinize the genital tubercle and genital swellings.

Therapy

All patients who have androgen insensitivity syndromes should undergo gonadectomy, the timing of which is controversial. Postpubertal gonadectomy enhances bone maturation as well as body development, but delaying the removal increases the risk of testicular malignancy. After the testes are removed, hormone therapy begins with estrogen re-

placement. Because of the short length of the vagina, some patients require vaginal lengthening. Most patients report satisfactory outcomes after vaginoplasty.

Psychological support probably is the most important aspect of care for affected patients. Psychosexual development in patients who have CAIS is female. Patients having this condition view themselves as being entirely female, as do other people. The overwhelming number of patients report being attracted to males. The resistance to testosterone does not appear to affect sexual drive adversely. Long-term psychological care should be provided to patients who have androgen insensitivity syndromes and their families by those trained in the fields of intersexuality and psychosexual development.

Lessons for the Clinician

Androgen insensitivity must be considered in the evaluation of girls who have primary amenorrhea or labial or inguinal masses and in patients who have ambiguous genitalia. This condition also should be suspected in infants who have inguinal or labial masses. A combination of karyotyping, hormone studies, and imaging allows definitive diagnosis. Treatment consists of removal of the testes and hormone replacement therapy in addition to the critical element of psychological support and counseling for patient and family. (*Pranita Tamma, MD, Claude Migeon, MD, Johns Hopkins School of Medicine, Baltimore, Md.*)

Reference

1. Wilkins L. *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*. Springfield, Ill: Charles C Thomas; 1950

Case 2 Discussion

Differential Diagnosis

Bilateral periorbital swelling in a child can result from nephrotic syndrome, orbital cellulitis, cavernous sinus thrombosis, or carotid-cavernous fistula. Other causes include angioedema, allergic dermatitis, ocular involvement of Graves disease, hypothyroidism, juvenile dermatomyositis, vasculitis, and malignancies such as chloroma (acute leukemia), lymphoma, and neuroblastoma.

The presence of discoloration over the swollen lids (Figure) is uncommon in nephrotic syndrome and Graves ophthalmopathy. Orbital cellulitis usually is painful and accompanied by fever. An allergic process is associated with prominent itching, and angioedema isolated to the eyes is uncommon.

In this child, history and findings on examination did not support a malignant process or a hypothyroid state. The confinement of the lesion to the preseptal area with normal eye movements, vision, and funduscopic findings argued against cavernous sinus disease. Vasculitis could not be ruled out on clinical grounds alone, but other organs usually are involved, accompanied by laboratory signs of inflammation. Although uncommon, juvenile dermatomyositis can present with isolated eye swelling together with a heliotrope rash in the absence of generalized muscle weakness. On careful examination, this patient had subtle neck weakness and muscle atrophy.

Laboratory Evaluation

Normal findings on urinalysis ruled out nephrotic syndrome. Orbital cellulitis was unlikely because the patient was afebrile, evaluation for infection was negative, and he did not respond to multiple antibiotics. Normal results on imaging studies ruled



Figure. Periorbital swelling and heliotrope rash before treatment was initiated.

out cavernous sinus pathology. Normal C1 esterase inhibitor and complement levels ruled out hereditary angioneurotic edema. Specific levels were: C1 esterase inhibitor, 18 mg/dL (0.18 g/L) (normal, 10 to 25 mg/dL [0.10 to 0.25 g/L]); C2, 2.5 mg/dL (0.25 g/L) (normal, 1 to 4 mg/dL [0.10 to 0.40 g/L]); C3, 128 mg/dL (1.28 g/L) (normal, 68 to 160 mg/dL [0.68 to 1.60 g/L]); and C4, 41 mg/dL (0.41 g/L) (normal, 16 to 64 mg/dL [0.16 to 0.64 g/L]).

Although the boy had skin reactions to multiple common allergens, the lack of response to appropriate treatment given for more than 1 month argued against an allergic cause. A normal thyroid profile ruled out thyroid causes. The normal results of bone marrow study and imaging studies ruled against a malignant process.

Central to the diagnosis was the finding of muscle weakness. A good clinical tool for assessing muscle strength, function, and endurance in

children who have myositis is the Childhood Myositis Assessment Scale (CMAS), devised by the Juvenile Dermatomyositis Disease Activity Collaborative Study Group (see Suggested Reading). This 14-item scale involves evaluation of tasks such as leg raising, sit-ups, and arm raising, with a timing element involved.

The elevated concentrations of muscle enzymes, including AST, LDH, CK-MB isozyme, and aldolase, supported a myopathic process. In association with his periorbital findings and neck weakness, dermatomyositis became the primary consideration. Although vasculitis can present with similar findings, the lack of other organ involvement and inflammatory markers did not support that diagnosis. Increased von Willebrand antigen activity, as evidence of endothelial activation, is common to both dermatomyositis and vasculitis.

A normal total CK level does not rule out myositis. CK values frequently normalize in untreated patients who have dermatomyositis af-

ter several months; concentrations of other muscle enzymes, including AST, ALT, LDH, and aldolase, may be elevated. Thus, all enzymes should be measured if myositis is suspected. CK-MB elevation with a normal total CK concentration may be seen in peripheral myositis due to regeneration and expression of primitive CK isoenzymes in muscle. von Willebrand factor antigen activity may be increased in dermatomyositis because of associated vascular injury (sensitivity 85%, specificity 45%). This finding can help differentiate dermatomyositis from polymyositis, which is characterized by pure muscle inflammation without vessel wall involvement.

A positive antinuclear antibody (ANA) titer can be useful in suggesting a rheumatologic condition. In this case, the ANA test result was negative, which occurs in 15% to 85% of cases of dermatomyositis, depending on the series.

MRI of the muscles is a sensitive and useful tool in the investigation of inflammatory muscle diseases. MRI can aid in finding a site for muscle biopsy because the myositic process often is patchy. A biopsy performed without the guidance of MRI can result in a false-negative outcome. MRI also can be useful in following the disease course.

On further investigation of this boy, MRI of the neck and thigh muscles showed an abnormal T2-signal intensity in the left sternomastoid muscle and patchy signals in proximal thigh muscles. A biopsy from the left sternocleidomastoid muscle showing marked endomysial and perivascular chronic inflammation with occasional small vessel wall infiltration along with degenerating and regenerating muscle fibers confirmed the diagnosis of juvenile dermatomyositis.

The Condition

Dermatomyositis is a vasculopathic (not vasculitic) disease of unknown cause that results in skin and muscle disease. Typical findings include a heliotrope rash around the eyes, proximal muscle weakness, periungual erythema from capillary abnormalities, and Gottron papules over knuckles and other extensor surfaces. Also called Gottron sign or Gottron nodes, these erythematous papules are found over the dorsal aspect of the metacarpopharyngeal and proximal interphalangeal joints of the fingers and on the extensor aspects of the elbows and knees. They may be pink and smooth, resembling melted wax, or scaly. The most common cutaneous manifestation of dermatomyositis, the lesions are caused by vascular ectasia with alternating dropout of the vessels.

Other manifestations of dermatomyositis include Raynaud phenomena, arthralgia, restrictive lung disease (muscle weakness and interstitial disease), abdominal pain, and involvement of the swallowing mechanism. Occasionally, ulcerations and perforation can occur in any part of the GI tract. A late complication in 40% of patients who have chronic dermatomyositis is the development of calcinosis.

About 40% of patients who have dermatomyositis have a monocyclic, limited disease; others have a chronic course. There is a 3% to 10% mortality rate, primarily in patients who have GI ulcerative disease or who develop respiratory failure or treatment complications.

The adult form of dermatomyositis commonly is associated with malignancy, unlike childhood disease. However, in this patient, who presented with cytopenia, it was prudent to rule out malignancy.

Therapy

Initial treatment consists of high doses of steroids (often started by intravenous [IV] pulses) and methotrexate. Other treatments include IV immunoglobulin, cyclosporine or tacrolimus, and cyclophosphamide for severe disease.

This patient was treated with pulse methylprednisolone, methotrexate, and IV immunoglobulin. Significant improvement was noted within 5 days. He was discharged on tapering doses of oral prednisone and continues to receive methotrexate and monthly IV immunoglobulin. Within 1 month, he had normal muscle strength, muscle enzyme levels, and von Willebrand antigen activity. He remains well 1 year later on maintenance treatment with a minimal dose of prednisone.

Lessons for the Clinician

Dermatomyositis should be included in the differential diagnosis of bilateral eyelid swelling, especially when there is an overlying rash. Absence of muscle weakness in the presence of the classic periorbital findings can be a presentation of dermatomyositis, a form called "amyopathic." As in this patient, a careful search for subtle weakness should be performed by using the CMAS, which is more sensitive than a traditional examination in detecting muscle weakness. MRI imaging and enzyme levels can be valuable in evaluating muscle function. Early aggressive treatment is warranted and may prevent complications such as calcinosis. (*Debabrata Ghosh, MD, Tobias Loddenkemper, MD, Bridget Wright, MD, Shannon Phillips, MD, Michael G. Levien, MD, Richard A. Prayson, MD, Philip Hashkes, MD, The Cleveland Clinic Foundation, Cleveland, Ohio*)

EDITOR'S NOTE. This case was selected from the 10 finalists in the 2005 Clinical Case Presentation program for residents held by the Resident Section of the American Academy of Pediatrics (AAP). Drs Ghosh, Loddenkemper, and Wright were residents when they wrote the case. Choosing which case to publish involved consideration of the teaching value and excellence of writing but also the content needs of the journal. Another case will be chosen from the 10 finalists presented at this year's AAP National Conference and Exhibition and published in 2007.—LFN

Case 3 Discussion

The patient's symptom of chest pain could have pulmonary, GI, cardiac, or psychogenic causes. However, the decreased breath sounds, dyspnea, and hypoxia implicated respiratory disease. Possible disorders included pneumothorax, pneumomediastinum, pulmonary embolism, and infection. The radiograph showed no evidence of pneumothorax or pneumomediastinum.

Additional history revealed that the patient was 6 months postpartum and was currently taking oral contraceptive pills. She smoked one-half pack of cigarettes each day. This information led to consideration of thrombosis and pulmonary embolism as well as infection. The predisposing factors for thrombosis in children and adults differ. In adults, risk factors include bed rest, heart disease, estrogen therapy, smoking, and surgery, all of which are potential contributors to the triad of endothelial injury, stasis of blood flow, and hypercoagulability (Virchow triad).

In children, the most common risk factors include central venous catheter placement, malignancy, cardiac (or other major) surgery, and infection, including sepsis. Thromboses in chil-

dren arise from the upper extremities in 60% of cases; the majority of clots in adults originate in the lower extremities. The clinical presentation of pulmonary embolus is the same, however, and includes tachypnea, tachycardia, dyspnea, pleuritic chest pain, cough, and sometimes hemoptysis.

The gold standard of diagnostic testing for pulmonary embolism remains pulmonary angiography. Because this modality is not always available and carries risks, physicians often turn to MR angiography or helical CT with IV contrast. Both of these tests currently have specificities greater than 90%. However, a negative CT scan does not rule out pulmonary embolism absolutely, particularly in a patient considered to be at high risk. Current recommendations are that patients who have signs and symptoms of pulmonary embolism together with ultrasonographic findings that show deep venous thrombosis should be treated.

The CT scan of this patient's chest showed no evidence of pulmonary embolism, yet confirmed the presence of bilateral pneumonia and small pleural effusions, making infection more likely. Despite therapy with ceftriaxone, her respiratory distress worsened. Intravenous azithromycin was added to address a possible "atypical pneumonia."

Community-acquired pneumonia refers to lower respiratory tract infection acquired outside the hospital and in adolescents often is caused by *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. "Atypical" is a term applied to pneumonia in patients who lack the typical symptoms and signs associated with pneumococcal infection (high fever, chills, productive cough). Infection with *C pneumoniae* is more common in children approximately 2 to 5 years of age. Infection with *M pneumoniae* has two peaks, the first between 5 and 9

years and the second in the early teen years. *C trachomatis* usually causes afebrile pneumonia in young infants 4 to 18 weeks of age. This patient had no history of exposure to psittacine birds such as parakeets and parrots, which is associated with *C psittaci* pneumonia.

Although *M pneumoniae* and *C pneumoniae* classically cause mild disease, they also can cause more serious complications, such as pleural effusion, pneumatocele, lung abscess, pneumothorax, and acute respiratory distress syndrome. First-line treatment for atypical pneumonia is a macrolide or an azalide. Serologic tests in this patient showed no evidence of infection by either organism.

An Unlikely Finding

Considering some of the more unusual causes of atypical pneumonia, a urinary antigen test for *Legionella pneumophila* was obtained, and results were positive.

Although *L pneumophila* is a rare pathogen in children, it is among the most commonly identified pathogens in community-acquired pneumonia in adults. This organism first was identified in 1976 during an outbreak of pneumonia among delegates to the American Legion convention in Philadelphia. Since that time, it has been found to be a relatively common cause of community-acquired pneumonia. Although there are more than 30 species of *Legionella*, approximately 90% of cases are caused by *L pneumophila*. Risk factors for nosocomial legionellosis are cigarette smoking, chronic lung disease, and immunosuppression. Most children who acquire Legionnaires' disease are immunosuppressed, usually by corticosteroids.

Transmission is by inhalation of aerosols containing *Legionella* or aspiration of water contaminated with the bacteria. The incubation period is 2 to 10 days, and the manifestations

most often include significant malaise with cough, chest pain, and fever. Cough can be accompanied by hemoptysis. In addition, GI symptoms are prominent and include watery, nonbloody diarrhea.

Diagnosis

It is difficult to distinguish Legionnaires' disease from other causes of community-acquired pneumonia on the basis of clinical findings. Laboratory studies may show renal and hepatic dysfunction, but more often show thrombocytopenia, leukocytosis, and hyponatremia (with a sodium level <130 mEq/L [130 mmol/L]). Fever usually occurs before the chest radiograph shows pulmonary infiltrate. The infiltrate does not distinguish Legionnaires' disease from other pneumonias, and the chest radiograph shows pleural effusions in approximately 33% of patients.

Definitive diagnosis is made most easily through urinary antigen testing. This enzyme immunoassay has both a high sensitivity and specificity. Although there are more than 14 serogroups of *L pneumophila*, more than 80% are caused by serogroup 1, which is the only serogroup detected by the urinary antigen test.

Therapy

Prompt treatment is important to reduce mortality. Azithromycin is the drug of first choice for children. Quinolones are recommended for therapy for persons 18 years of age or older. Rifampin can be added for patients who are immunocompromised or severely ill. Alternative drugs include doxycycline (in children 8 y or older) and trimethoprim-sulfamethoxazole. The recommended duration of therapy is 5 to 10 days for azithromycin and 14 to 21 days for the other drugs. Immunocompromised patients and those who are severely ill

require longer courses. All documented cases should be reported to state and local health departments.

Lessons for the Clinician

When evaluating a child who has cough, chest pain, and fever, espe-

cially if the patient is immunocompromised, clinicians should keep legionellosis in mind. Other clues to this infection include hyponatremia, pleural effusion, and diarrhea. Testing for *Legionella* is recommended for any patient hospital-

ized with enigmatic pneumonia. Urinary antigen testing is a valuable aid to diagnosis, and azithromycin is the drug of choice. (*Rebecca Dixon, MD, Indiana University Purdue University, Riley Children's at Methodist Hospital, Indianapolis, Ind.*)

In Brief

Colic

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Author Disclosure

Drs Fireman and Serwint did not disclose any financial relationships relevant to this In Brief.

Paroxysmal Fussing In Infancy, Sometimes Called "Colic." Wessel MA, Cobb JC, Jackson EB, Harris GS Jr, Detwiler AC. *Pediatrics*. 1954;14:421–435

A Systematic Review of Treatments for Infantile Colic. Garrison MM, Christakis DA. *Pediatrics*. 2000;106:184–190

Is Colic A Gastrointestinal Disorder? Gupta SK. *Curr Opin Pediatr*. 2002;14:588–592

A Framework and Strategy for Understanding and Resolving Colic. Karp H. *Contemp Pediatr*. 2004;21:99–114

All babies cry, but when is it too much, and when is it colic? Crying is a normal primitive protective reflex that serves as an alarm to alert parents to a problem and to get their attention. However, infants who have colic cry excessively without an identifiable need. Such babies are difficult to console and provoke much parental anxiety. Sleep is interrupted for both infant and care-

giver, and mothers experience increased risks of breastfeeding failure, postpartum depression, and marital conflict. When infants cry excessively, they are at a much greater risk of child abuse. Parents become desperate for resolution and accept advice and therapies from a wide variety of resources, including physicians, family, friends, the media, and the Internet. It is estimated that between 16% and 26% of all infants experience colic. Although colic occurs in all socioeconomic, racial, and ethnic groups with no sex preference, the cause remains unknown. Initially hypothesized to be gastrointestinal (GI), it is more likely to be multifactorial, with behavioral, social, and neurodevelopmental components.

As described by Wessel, colicky infants cry more than 3 hours per day, more than 3 days per week, and for more than 3 weeks. Excessive crying begins at 2 weeks of age, peaks at 6 weeks, may decrease by 8 weeks, and usually resolves completely by 16 weeks. It is interesting to note that preterm infants experience colic beginning 2 weeks past their due date. Crying spells are episodic, unrelated to feeding. Even though parental comforting may lessen the intensity, crying continues. The pattern is diurnal, with increased crying in the evening and night. Although all infants exhibit a similar pattern of fussiness in the evening that

peaks at 6 weeks of age, infants who have colic often are inconsolable for longer intervals and cry with more intensity. Babies who have colic draw up their legs while they cry, have tense abdomens, arch their backs, and are "gassy," which suggests a GI origin. Anytime a baby cries excessively, there is aerophagia or swallowing of air. Newborns swallow air immediately after birth and soon are gassy; this aerophagia continues for more than 4 months. The presentation of aerophagia and gas does not coincide with the timing of colic. Gas does not cause colic. Rather, the excessive crying that accompanies colic usually leads to aerophagia.

Diagnosis is made by history, complemented by normal findings on physical examination. Colicky infants otherwise are healthy and growing normally. Yet, it is important to consider other illnesses prior to diagnosing colic. Gastroesophageal reflux (GER), which can present with increased crying, often is suggested as causing colic. However, only 2% to 4% of infants who have symptoms of colic have been shown to have GER. Formula intolerance such as lactase deficiency or cow milk allergy often is implicated in the differential diagnosis, but is associated with additional symptoms such as emesis, diarrhea, blood in the stool, severe eczema, or urticaria. Laboratory tests, imaging,