

Letters to the Editor

Meeting the Iron Needs of Infants and Young Children

To the Editor: Despite the American Academy of Pediatrics' (AAP) strong endorsement of breastfeeding, most infants in the United States are fed some type of infant formula by the time they are two months old. Iron deficiency remains a nutritional problem among infants and young children in Saudi Arabia, although at present there is no national data available on infants at low risk.¹ The prevalence of iron deficiency anemia in the USA ranges from 3.5% for infants six months of age, 10.5% for those 18 months of age and 24.3% among infants between 10 and 14 months in low-income families.²

The AAP Committee on Nutrition³ has strongly advocated iron fortification for infant formula since 1969 as a way of reducing the prevalence of iron deficiency anemia and its attendant sequelae during the first year. In 1976, the second statement from the AAP, titled "Iron Supplementation for Infants,"⁴ delineated the rationale for iron supplementation, proposed daily dosage of iron, and summarized potential sources of iron in the infant diet. In 1989, the AAP Committee on Nutrition published a statement that addressed the issue of iron-fortified infant formulas, and concluded that there was no convincing contraindication to iron-supplemented formulas, and that continued use of low-iron formulas posed an unacceptable risk of iron deficiency during infancy.⁵ The conclusion of the Nutrition Committee of the Canadian Pediatric Society⁶ in 1991 was along the lines of the American Academy of Pediatrics' recommendations. Recent recommendations of the AAP Committee on Nutrition for iron fortification of infant formulas continue to strongly urge fortifying infant formula with iron.⁷ Their recommendations can be summarized as follows:

1. As recommended earlier, in the absence of underlying medical factors (which are rare), human milk is the preferred feeding for all infants.
2. Infants who are not breast-fed or are partially breast-fed should receive an iron-fortified formula (containing between 4-12 mg/L of iron) from birth to 12 months.
3. The manufacture of formulas with iron concentration of less than 4 mg/L should be discontinued. If such formulas continue to be manufactured, low-iron formulas should be prominently labeled as potentially nutritionally inadequate, with a warning specifying the risk of iron deficiency. These formulas should not be used to treat colic, constipation, cramps or gastroesophageal reflux.
4. If low-iron formulas continue to be manufactured, iron-fortified formulas should have the term (with iron) removed from the front label.

5. Parents and health care clinicians should be educated on the role of iron in infant growth and cognitive development, as well as the lack of data about negative side effects of iron and current fortification levels.

In summary, the 1999 statement of the AAP Committee on Nutrition represents a scientific update of the 1976 and 1989 statements with recommendation on the use of iron-fortified and low-iron formula in term infants. Milk formulas in Saudi Arabia and the Gulf region are obtained from around the world. It would be a safe practice for both parents and physicians to ignore the label of "iron fortified" and read the contents. The Infant Formula Act requires that formulas fortified with greater than 6.7 mg/L iron be considered labeled as "iron fortified."

Souheil Shabib, MD, FRCPC, FAAP

Consultant, Pediatric Gastroenterology/Nutrition
Medical Director, Nutrition Support Unit, MBC-58
King Faisal Specialist Hospital and Research Centre
P.O. Box 3354
Riyadh 11211, Saudi Arabia

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Vascular Thrombosis in Newborn Infants

To the Editor: I read with interest the brief report titled "Vascular Thrombosis in Newborn Infants" by Al-Omran and Al-Alaiyan,¹ and was surprised that the authors had not mentioned the extent to which inherited thrombophilia and antiphospholipid antibodies had been investigated. Not every preterm infant with central catheter and sepsis will develop thrombosis; one or more risk factors may co-exist.² In a review of thrombotic disorders in the newborn,³ intravascular catheter was the most common risk factor, primarily because inherited thrombophilia, especially the newer commonly described conditions such as activated protein C-resistant (APCR) and prothrombin mutation (PTM), were not tested for. A recent study performed in a different population of pediatric patients showed that 38% of children with cerebral thromboembolism had inherited thrombophilia and/or antiphospholipid antibodies.⁴ Another

study suggested that factor V Leiden mutation plays a role in the development of arterial and venous thrombosis in neonates and children.⁵

Many abnormalities in hemostatic proteins have been suggested to be prothrombotic, however, there is currently evidence supporting the prothrombotic nature of clinical significance for only the following inherited conditions: deficiency of antithrombin III, protein C and protein S, APCR, PTM (20210 G to A), hyperhomocysteinemia, dysfibrinogenemia, and possibly raised factor VIII and raised fibrinogen level.^{6,7} APCR and PTM are fairly common in Western populations, occurring in 5% and 1%, respectively. It is advisable to test patients with thrombosis for these conditions to provide future prophylaxis and family screening.⁶ The normal range of some hemostatic proteins is not well known in newborn and young children due to the ethical difficulty of bleeding healthy subjects to establish normal range. Moreover, these proteins are consumed in thrombosis and measurements in acute events may not reflect the baseline level. Fortunately, molecular testing is available for the most common inherited thrombophilia, APCR and PTM, where age or recent thrombosis does not affect these tests. Antiphospholipid antibodies are an acquired prothrombotic condition commonly seen as a transient phenomenon in children following viral infections. Preterm babies may not be able to mount this immune response, and the passage of antibodies from maternal circulation should be considered.⁸

A family history of thrombosis and even the testing of parents for inherited thrombophilia may throw more light on the presence of such thrombophilia in preterm infants who need ITU care and intravascular catheter. The benefits of these measures will be substantiated by the presence of standard prophylactic protocols similar to those used for adults.⁹ Such protocols have not yet been established for neonates and young children.¹⁰

Khaled A.B. El-Ghariani, MD

Department of Haematology
Leicester Royal Infirmary
Leicester, LE1 5WW
U.K.

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Reply

To the Editor: We would like to thank Dr. El-Ghariani for his comments. Our study on vascular thrombosis in newborn infants was retrospective. The available data with respect to the etiology of the thrombosis was obtained from the infant's record. In the absence of universal guidelines for the management of neonatal thrombosis, a complete investigation for the disease will not be accomplished. Furthermore, the disease has a multifactorial nature, which is clearly seen by the frequent description of one or more predisposing genetic and/or environmental risk factor in affected patients. Although the disease has numerous risk factors, the term "thrombophilia" refers only to the familial or acquired disorders of the hemostatic system that result in thrombosis. Most of the genetic defects affect the function of the natural anticoagulant pathways that play a role in the pathogenesis of the inherited thrombophilias. The genetic defects include antithrombin III deficiency, resistance to activated protein C (APCR), protein C and protein S deficiencies, as well as the rare form of dysfibrinogenemia. The investigation of these genetic defects during thrombosis is inaccurate. Unfortunately, more sophisticated tests such as molecular testing for these inherited thrombophilia are not available in all laboratories. These difficulties, coupled with the absence of guidelines for the management of neonatal thrombosis, prompt health care professionals to focus mainly on the diagnosis and treatment.

Saleh Al-Alaiyan, MD, FRCPC

Head, Section of Neonatal Intensive Care
Department of Pediatrics, MBC-58
King Faisal Specialist Hospital and Research Centre
P.O. Box 3354
Riyadh 11211, Saudi Arabia

Pyogenic Spinal Epidural Abscess

To the Editor: I read with interest the article "Pyogenic Spinal Epidural Abscess" by Al-Othman et al.,¹ reporting four cases of this rare lesion. Pyogenic spinal epidural abscess is a true surgical emergency, and its potential for permanent neurologic damage makes early diagnosis and prompt therapy of extreme importance. The rate of

mortality of adults ranges from 18% to 25%.^{2,3} Unfortunately, accurate diagnosis at the time of admission is the exception rather than the rule. Only 20% of epidural abscesses are recognized at the time of hospital admission. The common presenting features are backache (72%), radicular pain (47%), weakness of an extremity (35%) bladder and bowel dysfunction (30%), sensory deficit (23%), and frank paralysis (21%).⁴ Atypical presentation that developed only after having moved heavy household items has also been reported in patients presenting for evaluation.⁵ Therefore, its possibility should always be kept in mind when evaluating a case of back pain.

The authors used CT scan instead of MRI, although the latter is now considered to be the radiologic procedure of choice for the detection of epidural abscess due to its higher specificity. Gadolinium-enhanced MRI is essential for the diagnosis of abscess without frank pus formation in defining the extension of infection and in assessing the therapeutic effects.⁶ It has superior ability to demonstrate associated mass effect upon the cauda equina and potential signal abnormalities within the discs, vertebral bone marrow and spinal cord. The addition of an intravenous gadolinium-contrast agent better defines central necrosis suggestive of abscess rather than cellulitis. MRI offers the additional advantage of not requiring a lumbar puncture. If MRI is unavailable, CT with myelography usually provides adequate information. A normal CT alone does not exclude the diagnosis of epidural abscess. The reader would have appreciated the inclusion of photographs of CT scans in this article due to the rarity of this disorder.

Surgical decompression was once thought to be mandatory in all cases. Now, early diagnosis by MRI scans allows for effective medical therapy prior to occurrence of neurologic compression. But in the case of medical management, the patient should be closely monitored by serial studies with MRI because of a potential risk of sudden neurological deterioration.⁷ The chances of recovery relate inversely to the amount of neurologic dysfunction at the time of diagnosis. Long-term outcome after the surgical and/or medical treatment can be predicted with the use of a simple grading system (Grades 0-III), based on patient age, degree of thecal sac compression, and duration of symptoms.⁸

Suresh K. Dargan, MBBS, MS(Ortho)

Department of Orthopedics
Government General Hospital
Rafha, North Zone
Saudi Arabia

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Reply

To the Editor: I would like to thank Dr. Dagan for his comments, and wish to state that only CT scan was available at the time of the presentation of our cases. I agree with Dr. Dagan that MRI is more useful in the diagnosis as well as the long-term follow-up of spinal epidural abscess, depending on the duration of symptoms, severity of cord compression, as well as the age of the patient.

Abdullah Al-Othman, MBS, FRCS

Associate Professor, Consultant Orthopedic Surgeon
King Fahd University Hospital
P.O. Box 2845
Al-Khobar 31952, Saudi Arabia

***Cryptosporidium* Gastroenteritis in Four Immuno-competent Children Presenting with Features of Intestinal Obstruction**

To the Editor: The worldwide epidemic of AIDS has stimulated medical interest in the coccidian parasite *Cryptosporidium*, which causes severe gastroenteritis (GE) in up to 50% of such patients.¹ The first human *Cryptosporidium* GE was reported in 1976,² and until the early 1980s, only seven cases had been reported, five of which were in immunosuppressed patients.¹ More recently, large outbreaks of *Cryptosporidium* GE in immuno-competent individuals, due to water supply contamination, have been reported in the USA.³⁻⁵ The parasite is resistant to water chlorination, and is transmitted via the orofecal route and close contact with infected humans or animals.³ The parasite is now considered to be the third most common cause of infective diarrhea in children of the developing world, where it may cause malnutrition as well.³ We report *Cryptosporidium* GE with features of intestinal obstruction in four Saudi children. These are the first reported cases in Saudi Arabia to our knowledge.

Case Reports

Case 1

A 6-year-old male child presented with a three-day history of watery diarrhea, abdominal cramps and four episodes of bilious vomiting. Upon examination, he was mildly dehydrated with moderate abdominal distention and normal bowel sounds. He had x-ray features of intestinal obstruction (Figure 1). His stools were positive for *Cryptosporidium* oocysts.

Case 2

A seven-year-old male child was referred by the surgeon on call with a 12-day history of watery diarrhea, bilious vomiting, abdominal pain and mild fever. A sister had had GE two weeks previously. The patient appeared healthy but mildly dehydrated, and his abdomen was moderately distended and mildly tender. His bowel sounds were present, and x-ray showed evidence of intestinal obstruction. The patient's stools were positive for *Cryptosporidium* oocysts.

Case 3

A 3½-year-old male child had a five-day history of watery diarrhea, vomiting, abdominal distention and crampy abdominal pain. His mother had had GE two weeks previously. He was pale and mildly dehydrated. His abdomen was distended with normal bowel sounds. Abdominal x-ray showed evidence of intestinal obstruction. His stool and that of an asymptomatic brother were positive for *Cryptosporidium* oocysts. He also had sickle cell trait (HbAS).

Case 4

A two-year-old girl was referred by the surgeon as having a two-day history of frequent watery diarrhea, mild fever, bilious vomiting, abdominal pain and distention. Her temperature was 39.5°C, and she was moderately dehydrated. She had abdominal distention and mild diffuse abdominal tenderness with sluggish bowel sounds. X-ray showed evidence of intestinal obstruction. Her stool was positive for *Cryptosporidium* oocysts.

Overview of Cases

In the period of January to March 1999, four children were admitted with acute GE. They ranged in age between two and seven years, and comprised three males and one female. All four had acute watery diarrhea for 2-12 days with no mucous or blood. All four had frequent vomiting, three of whom had bile-stained vomitus. All four had abdominal distention, crampy abdominal pain and x-ray features of intestinal obstruction (gaseous bowel distention with multiple fluid levels). Two (cases 2 and 4) were initially admitted under surgical care and the other two had surgical consultations, but all four had medical treatment only. One patient (case 4) had a fever of 39.5°C. In all four, the dehydration was mild to moderate and responded to IVF

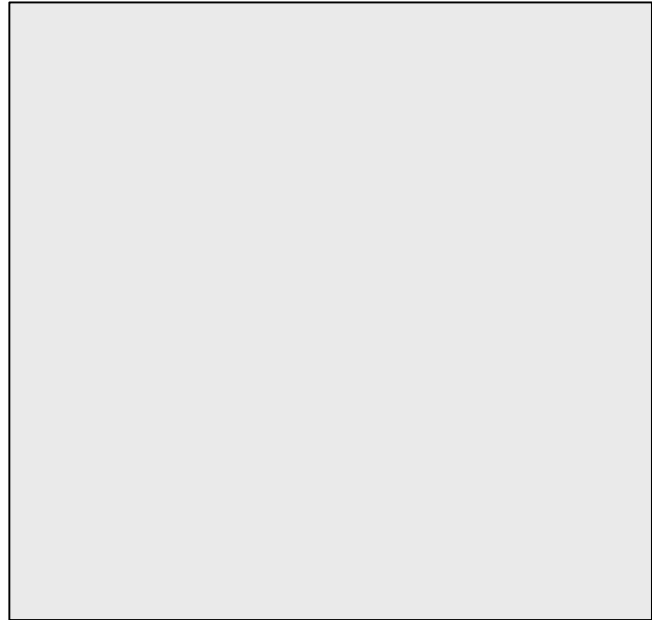


FIGURE 1. Erect x-ray abdomen of case 2 showing gaseous distension of bowel and multiple fluid levels.

therapy. Routine stool analysis was negative, however, the modified Kinyoun acid-fast stain was positive for *Cryptosporidium* oocyst in all four.⁶

All four children had normal serum potassium U&E, CBC and immunoglobulins, and HIV testing was negative. Water-supply testing for oocysts was negative in the four households. An asymptomatic brother of case 3 had oocysts in his stool, while the rest of the contacts tested were negative. All four children and the asymptomatic brother of case 3 were treated with azithromycin 10 mg/kg/day for five days, and all had negative stool after treatment.

Discussion

Cryptosporidium GE in immunocompetent patients is known to be mild, as in the case of these four children described, and may even be a self-limiting disease.³ However, in an immunosuppressed person, besides the persistent enteritis, the parasite can cause severe invasive disease in the form of pneumonia, cholecystitis, pancreatitis, and may even end fatally, as there is no effective treatment.^{1,3,7,8}

The prevalence of the disease in the developing world is not yet known because the parasite is not detectable by routine stool testing. It has been reported that up to 45% of Israeli Bedouin infants get the infection by the age of two years.⁹ The extent to which the parasite infection is implicated as a cause of malnutrition has yet to be decided by more investigations.

It is interesting that all four cases studied presented with features of intestinal obstruction. Apart from one case of gastric obstruction due to *Cryptosporidium* in a child with

congenital HIV,¹⁰ we could find no literature reference of intestinal obstruction caused by the parasite. As to how the infection with the parasite causes intestinal and/or gastric obstruction, one can only postulate that at the initial infective stage where the parasite attaches itself to the enterocytes of the villi, it produces paralysis of the small intestine, probably through a chemical mediator, in order to escape being expelled by the bowel movement. Further studies are needed to find out the exact pathophysiology of this infection. However, clinicians should have a strong index of suspicion to avoid subjecting such children to unnecessary surgical procedures. We recommend that children presenting with GE and features of intestinal obstruction, and those with chronic diarrhea, especially if they are malnourished or immunosuppressed, should have their stools tested for the parasite.

The rapid response of these four children to azithromycin indicates that the drug may be effective in treating both the disease and carrier state, however, the number presented is not enough to enable one to draw such conclusions, and more studies would be needed.

M.A. Malik, FRCPC, MRCP, DCH

Chief of Pediatrics

King Abdulaziz Hospital and Oncology Center

P.O. Box 31467

Jeddah 21497, Saudi Arabia

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