Evidence-Based Answer

A single CRP value cannot diagnose or predict serious bacterial infections (SBI) in neonates. However, serial negative CRP values rule out SBI with a high degree of certainty (SOR: A, prospective cohort studies).

A prospective cohort study (n=1,136) evaluated the effectiveness of serial CRP levels to predict serious bacterial infection (SBI) in hospitalized neonates. Standardized clinical pathways were used and CRP levels were drawn at initial presentation and on the next 2 mornings. One hundred fifty-nine infants either had proven (culture-positive) or probable (positive clinical and/or laboratory findings) sepsis.

When using 1 mg/dL as a cutoff, the sensitivity for proven or probable sepsis for CRP#1 and serial CRP (1 of 3 values positive) was 39.4% and 97.8%, respectively (negative likelihood ratio [LR–] 0.66 and 0.03). Specificity for CRP#1 and serial CRP was 92.5% and 76.3%, respectively (positive likelihood ratio [LR+] 5.3 and 4.1). The authors concluded the sensitivity of a normal CRP value is insufficient to withhold antibiotic treatment in suspected SBI, whereas 2 CRP values <1 mg/dL obtained 24 hours apart made sepsis highly unlikely.

A prospective cohort study (n=401) assessed the predictive value of 9 clinical signs of sepsis (eg, feeding intolerance, apnea, bradycardia, abdominal distension) and CRP in neonates ≤28 days admitted for suspected SBI. Logistic regression was used to associate these signs with CRP in confirmed cases (culture proven) of SBI. At inclusion, CRP levels were measured once daily for 4 days. Eighty-three (21%) neonates had positive blood cultures, of which 81 had CRP levels available. The initial CRP value was positive (≥1 mg/dL) in 93% of neonates with culture-proven sepsis (sensitivity 93%; specificity 27%; LR– 0.26; LR+ 1.3). The authors recommended the diagnosis of SBI should be based on a combination of criteria and not on CRP value alone.

The Centers for Disease Control and Prevention guidelines for prevention of early-onset group B streptococcal disease in newborns do not consider acute-phase reactants part of the diagnostic evaluation for suspected SBI. The National Institute for Health and Clinical Excellence guidelines from the United

-period. Among the 484 (61%) women who responded, a lack of vaginal lubrication during the first 3 months after giving birth was reported at higher rates than during the year prior to the pregnancy (46% vs 12%; P<.001).

A cohort study with 215 women at their 4-week postpartum visit explored the relationship among vaginal pH, vaginal atrophy, and the effect of estrogen therapy. All women underwent an extensive gynecologic history and specialized vulvar/vaginal exam (vestibular cotton swab test, vaginal wall cytology, vaginal wall wet mount, assessment of vaginal tenderness with gentle wall scraping) and measurement of vaginal pH. Thirty-seven women (17%) were diagnosed with vaginal atrophy based on a pH ≥5.3 along with one symptom or one exam finding consistent with vulvar atrophy. A comparison group of 80 patients without vaginal atrophy was selected. There was a higher rate of breastfeeding in the atrophy group (68% vs 32%; P<.001). Dyspareunia was also more common in women with atrophy than those without (80% vs 14%; no P value given). All patients with atrophy were treated with conjugated estrogen vaginal cream 2 g twice a week for up to 40 days, at which point their vaginal pH had dropped below 5.3. No information was provided on whether symptoms were relieved.

In a case report of a 23-year-old primiparous woman at 13 months postpartum, the patient was diagnosed with lactational atrophic vaginitis. The authors reported noticeable improvement in her dysuria, vaginal itching and dryness, and severe pain with intercourse after 2 weeks of treatment with twice- to thrice-weekly 17 beta-estradiol estrogen cream.

In a narrative review, postpartum vaginal dryness was noted to be caused by a relative estrogen-deficient state that may be exacerbated by lactation. The review authors recommended topical estrogen, as well as medications typically used for postmenopausal vaginal atrophy—lubricants, vitamin E oil, and botanicals such as phytoestrogens, black cohosh, dong quai, and ginseng.

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Kingdom recommend continued CRP testing with other laboratory investigations when evaluating febrile neonates.4

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Should a 6-week-old infant exposed to chickenpox in a sibling receive varicella-zoster immune globulin (VZIG) or acyclovir?

Evidence-Based Answer

In an otherwise healthy 6-week-old infant exposed to chickenpox, the use of acyclovir or varicella-zoster immune globulin (VZIG) is not recommended, even though acyclovir does decrease the chance of infection (SOR: C, expert opinion).

A small RCT (from 1993) of 50 infants and children (4 months to 9 years of age) evaluated the use of acyclovir or placebo for the prevention of varicella after household exposure.1 The group treated with acyclovir received 40 or 80 mg/kg daily in 4 divided doses. Treatment was started on day 7 to 9 after exposure to the index case and continued for a total of 7 days. All subjects were examined approximately 14 days after index case exposure.

In the placebo group, all patients showed clinical signs of varicella; 25 (100%) developed a vesicular rash and 17 (68%) developed fever. Varicella developed in 4 of the 25 subjects (16%) receiving acyclovir ($P<.01$ compared with placebo) and only 1 reported fever. The severity of the skin rash was also less severe in the acyclovir group compared with the placebo group. The study’s authors concluded that varicella can be prevented or modified by administration of oral acyclovir late in the incubation period.1

Nevertheless, according to a 2009 statement by the American Academy of Pediatrics (AAP) on infectious disease, VariZIG (which replaced VZIG) and acyclovir are indicated only for a select group of patients if “significant exposure” has occurred.2 Significant exposure includes face-to-face indoor play and infants residing in the same household as a person deemed contagious. Contact should be nontransient—some experts say at least 5 minutes while others require at least 60 minutes. Candidates for treatment who meet exposure criteria include the following:

- immunocompromised children without history of varicella or varicella immunization
- pregnant women without evidence of immunity
- a newborn infant whose mother had onset of chickenpox within 5 days before delivery or within 48 hours after delivery
- a hospitalized preterm infant ($\geq$28 weeks) whose mother lacks a reliable history of chickenpox or serologic evidence of protection against varicella
- a hospitalized preterm infant ($\leq$28 weeks’ gestation or birth weight $\leq$1,000 g), regardless of maternal history of varicella virus serostatus

The AAP states that VariZIG should be administered as soon as possible and no later than 96 hours after exposure. There is no recommendation to use VariZIG or acyclovir in healthy term infants exposed to varicella.

In 2007, the Centers for Disease Control published the Advisory Committee on Immunization Practices’ recommendations for the use of VariZIG for postexposure prophylaxis for chickenpox.3 VariZIG was not recommended for normal-term infants exposed postnatally, even if their mothers had no prior history of varicella immunity. The authors stated that the risk of severe disease did not seem to be higher in this group than in other children.

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