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CME TEST
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Update of GBS screening guidelines

Bottom line

Implementation of universal screening of pregnant women at 35 to 37 weeks’ gestation significantly decreases early-onset group B streptococcal disease in neonates. Emerging evidence in the management of pregnant women with unknown group B Streptococcus (GBS) status, women with preterm labor, and women with preterm premature rupture of membranes (pPROM) suggests that morbidity and mortality could be reduced further if intrapartum screening methods were implemented.

Key changes in the 2010 guidelines include (1) standardization of laboratory methods for identification of GBS, (2) a colony-count threshold for reporting GBS detected in urine, (3) an updated algorithm for GBS screening and intrapartum antibiotic prophylaxis (IAP) in women with preterm labor and pPROM, (4) dosage changes for penicillin G used as IAP, (5) updated regimens for women allergic to penicillin, and (6) a revised approach for secondary prevention of early-onset GBS disease in newborns.

Evidence summary

Early-onset GBS disease continues to be a leading cause of neonatal morbidity and mortality in the United States, with a 4% to 6% mortality rate.¹ The implementation and revision of GBS screening programs from 1992 to 2010 has decreased the incidence of early-onset disease: for every 1,000 live births, there were 1.7 cases in 1993, 0.6 cases in 1998, and 0.34 cases in 2002.²³

A multistate, retrospective cohort study from a population of more than 800,000 live births evaluated universal screening for GBS based on 2002 national screening guidelines versus consensus guidelines from 1996 recommending IAP on the basis of risk alone. The study included 254 infants with GBS disease and 7,437 infants without GBS disease. The rate of screening was 48.1% (95% CI, 46.7–49.5) in 1998–1999 compared with 85% (95% CI, 83.9–86) in 2003–2004. A key finding was that mothers who delivered preterm were less likely to be screened (RR=0.56; 95% CI, 0.51–0.62) or receive IAP (RR=0.81; 95% CI, 0.75–0.87) than mothers delivering at term. Also, despite improvements in universal screening protocols, 61.4% of term infants with early-onset GBS disease were born to mothers who tested negative for GBS.³ This population-based approach highlighted the importance of identifying
In Depth

**TABLE**

<table>
<thead>
<tr>
<th>Indications for Intrapartum Antibiotic Prophylaxis</th>
<th>Nonindications for Intrapartum Antibiotic Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intrapartum GBS Prophylaxis Indicated</strong></td>
<td><strong>Intrapartum GBS Prophylaxis Not Indicated</strong></td>
</tr>
<tr>
<td>Previous infant with invasive GBS disease</td>
<td>Colonization with GBS during previous pregnancy</td>
</tr>
<tr>
<td>GBS bacteriuria during any trimester of the current pregnancy (concentration ≥10⁴ colony-forming units/mL)</td>
<td>GBS bacteriuria during previous pregnancy</td>
</tr>
<tr>
<td>Positive GBS vaginal-rectal screening culture in late gestation (35–37 weeks) during current pregnancy</td>
<td>Negative GBS vaginal-rectal screening culture in late gestation (35–37 weeks), regardless of intrapartum risk factors</td>
</tr>
<tr>
<td>Unknown GBS status at onset of labor and any of the following: • Delivery at &lt;37 weeks' gestation • Amniotic membrane rupture ≥18 hours • Intrapartum temperature ≥100.4°F (≥38.0°C) • Intrapartum NAAT positive for GBS</td>
<td>Cesarean section performed before onset of labor for a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age</td>
</tr>
</tbody>
</table>

*a* Intrapartum antibiotic prophylaxis not indicated in this circumstance if cesarean section is performed before onset of labor for a woman with intact amniotic membranes.

*b* If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent active against GBS should replace GBS prophylaxis.

*c* NAAT testing for GBS is optional and might not be available in all settings. If intrapartum NAAT is negative for GBS but any other intrapartum risk factor is present, then intrapartum antibiotic prophylaxis is indicated. NAAT = nucleic acid amplification tests.

Factors that contributed to false-negative results (transient colonization or specimen processing issues) and a need for guidelines that address screening more than 5 weeks from the anticipated due date.

**Updated guidelines from the CDC**

A guideline working group convened in 2009, representing the ACOG, the AAP, the AAFP, the ACNM, the ASM, and the CDC. Their recommendations have been accepted by the sponsoring organizations and are published in the CDC’s Morbidity and Mortality Weekly Report. Outlines of the new recommended screening and treatment algorithms are shown in FIGURES 1 AND 2 (page 3).

**Antibiotic considerations**

Indications for IAP are listed in the TABLE. Penicillin G (5 million units IV initial dose, then 2.5 million–3 million units every 4 hours until delivery) remains the IAP drug of choice.

In a prospective observational study of 2,111 women in late third trimester, researchers conducted GBS antibiotic susceptibility testing on all patients. The GBS cultures had 100% susceptibility to vancomycin; 98% susceptibility to penicillin, ampicillin, and cefazolin; 92% susceptibility to clindamycin; and 81% susceptibility to erythromycin. The guidelines state that penicillin-allergic women not reporting anaphylaxis, angioedema, respiratory distress, or urticaria should be given cefazolin. Women with a severe penicillin allergy should receive clindamycin. If bacterial susceptibility testing in a highly penicillin-allergic patient reveals a strain of GBS that is resistant to clindamycin (or sensitivities are unavailable at the time of labor), vancomycin is recommended.

Ampicillin (2 g IV initial dose, then 1 g every 4 hours) is adequate GBS prophylaxis and appropriate latency antibiotic coverage for pPROM. Adequate IAP is 4 hours before delivery; IV penicillin, ampicillin, or cefazolin are the only antibiotics adequate for purposes of neonatal management.

**Specimen collection and processing**

The gold standard for GBS colonization remains vaginal-rectal cultures obtained between 35 and 37 weeks’ gestation. Polymerase chain reaction (PCR) for rapid detection of GBS has become available, but has not been widely adopted in the intrapartum setting.

Limitations of PCR include availability of testing, delay of results and antibiotic administration, and no antimicrobial susceptibility testing for penicillin-allergic women.

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**REFERENCES**

1. Tumbaga PF, Philip AGS. Neoreviews. 2006; 7(10):e524–e530. (LOE 5)
FIGURE 1

GBS screening and treatment algorithm for women with preterm labor

<table>
<thead>
<tr>
<th>Patient admitted for signs and symptoms of preterm labor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtain vaginal-rectal culture and start GBS prophylactic antibiotics</td>
</tr>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>Is patient entering true labor?</td>
</tr>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>Continue GBS prophylaxis until delivery</td>
</tr>
<tr>
<td>If culture returns negative, discontinue antibiotics</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
</tr>
<tr>
<td>Obtain GBS culture results</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
</tr>
<tr>
<td>GBS prophylaxis at onset of true labor</td>
</tr>
</tbody>
</table>


FIGURE 2

GBS screening and treatment algorithm for women with pPROM

<table>
<thead>
<tr>
<th>Obtain vaginal-rectal culture and start antibiotics for latency* or GBS prophylaxis</th>
</tr>
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<tbody>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>Is patient entering true labor?</td>
</tr>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>Continue GBS prophylaxis until delivery</td>
</tr>
<tr>
<td>Or Continue antibiotic for 48 hours if receiving for GBS prophylaxis†</td>
</tr>
<tr>
<td>Obtain GBS culture results</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>GBS prophylaxis at onset of true labor</td>
</tr>
</tbody>
</table>

*Antibiotics given for latency in the setting of pPROM that are adequate GBS prophylaxis include ampicillin 2 g IV once, followed by 1 g IV every 6 hours for at least 48 hours. If other regimens are used, GBS prophylaxis should be initiated in addition.
†GBS prophylaxis should be discontinued at 48 hours for women with pPROM who are not in labor. If results are negative before 48 hours, GBS prophylaxis should be discontinued.

Diving for PURLs

How do we pick PURLs?
We scour sources that cover 500 journals daily for useful research evidence, and meet weekly to critically appraise and discuss studies that meet our criteria. Here are our criteria:

- Relevant: Is the topic relevant to family medicine?
- Valid: Are the findings scientifically valid?
- Change in practice: Would this change practice?
- Medical care setting: Is this implementable in clinic, etc?
- Implementable: Can we implement this immediately?
- Clinically meaningful: Are results clinically meaningful?

Pressurized oxygen and room air have similar benefit in refractory dyspnea


This RCT assigned patients with refractory dyspnea (PaO₂ >7.3 kPa or 55 mmHg) and a terminal illness to either pressurized oxygen or pressurized room air via nasal cannula at 2 L/min for 7 days. Among those excluded were patients meeting requirements for long-term oxygen therapy (eg, PaO₂ <55 mmHg). The primary outcome was breathlessness on a validated numerical rating scale. Both groups improved from their baseline, but there were no significant differences between the oxygen and the room air groups in degree of breathlessness.

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Bottom line: It is unclear what mechanism is at work in the benefits seen here, and how much the content of the gas matters. Other evidence suggests that opioids may provide superior relief for intractable dyspnea in the terminally ill, but this issue was not addressed in this study. More research is needed to guide clinical decision making; these results do not provide adequate guidance in deciding among pressurized oxygen, pressurized room air, and/or opioids.

Tiotropium as good as salmeterol for asthma uncontrolled with an inhaled steroid


This study enrolled 289 patients with uncontrolled asthma into a blinded crossover trial that compared beclomethasone, tiotropium, and salmeterol. During a 4-week run-in period, all patients received inhaled beclomethasone 80 mcg BID, which was continued or increased in all patients after randomization. Patients received 1 of 3 treatments:

1. Beclomethasone plus tiotropium (18 mcg daily) plus placebo (in place of salmeterol)
2. Beclomethasone plus placebo (in place of tiotropium) plus salmeterol (50 mcg daily)
3. Double-dose of beclomethasone plus placebos (in place of tiotropium and salmeterol)

Each patient received a treatment arm for 14 weeks, followed by a 2-week washout period, after which they received another treatment. This cycle was repeated twice so that each patient received all 3 treatment arms.

Tiotropium and salmeterol both had small but statistically significant improvements in asthma symptoms when used with an intermediate dose of beclomethasone compared with high-dose beclomethasone alone. However, none of the 3 treatment arms had a clinically significant impact on symptoms scores.

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Bottom line: Tiotropium may be another treatment option for inadequately controlled asthma in conjunction with an inhaled glucocorticoid that appears to be equivalent to double-dose inhaled steroids or inhaled salmeterol. However, it is not clear to us that tiotropium should replace long-acting beta-agonists, because the long-term safety of tiotropium (particularly in asthma) has not been examined.

Article Reviewer and Summary Author: Kate Rowland, MD

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Article Reviewer and Summary Author: Kate Rowland, MD
Avoid zolpidem during pregnancy

This case-control study gathered data from a Taiwanese birth registry, comparing 2,497 women who received zolpidem during pregnancy with 12,485 women who did not. Outcomes were rates of low birth weight (LBW), Caesarean section, small size for gestational age (SGA), congenital anomalies, and preterm births.

The odds ratio for congenital anomalies was not significantly different between groups. For women who received zolpidem during pregnancy, the adjusted odds ratio (AOR) for LBW was 1.39 (95% CI, 1.17–1.64), for preterm birth was 1.49 (95% CI, 1.28–1.74), for SGA was 1.34 (95% CI, 1.20–1.49), and for Caesarean section was 1.74 (95% CI, 1.59–1.90). Similar results were found for women receiving the medication during the first trimester, compared with the second and third trimester, suggesting that zolpidem is not teratogenic. Likewise, the total number of days on zolpidem did not matter; similar AORs were found for women who used zolpidem for 30–90 days, 90–180 days, and more than 180 days.

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Shoe inserts for plantar fasciitis pain

Background
Plantar fasciitis (PF) heel pain affects up to 10% of the US population and is responsible for more than 600,000 ambulatory care visits annually. Shoe inserts (confusingly referred to as both orthotics and orthoses throughout the literature) are commonly discussed in the treatment of PF pain. Over-the-counter shoe inserts (OTC-SI) cost up to $50.00 and custom-made shoe inserts (CM-SI) cost up to several hundred dollars. Given the cost differences—and the difficulty in getting American insurance companies to help cover them—understanding the evidence behind the use of these 2 treatment modalities is worthwhile.

Review of the evidence
Evidence unclear about value of shoe inserts
A 2008 Cochrane review of 5 RCTs including 691 participants did not find clear evidence that CM-SI were effective in alleviating PF pain, neither in the short term (after 2 weeks of use) nor in the long term (up to 52 weeks). In these trials CM-SI were compared with OTC-SI, sham shoe inserts (a placebo), and night splints that stretch the Achilles tendon.

Meta-analysis suggests shoe inserts alleviate PF pain
However, a subsequent meta-analysis of 6 randomized trials and prospective cohort trials that included 277 participants reached a different conclusion. Each of these trials studied a different type of shoe insert (mainly arch supports and heel cups). Both OTC-SI and CM-SI were represented. Unfortunately, none of the 6 trials included a true control group (ie, a “no treatment” arm or a placebo treatment arm). Consequently, the authors chose a historic control group derived from a study of night splint treatment (and one of the RCTs included in the Cochrane review), which was reportedly 17% effective (95% CI, 8.9–25) at improving PF pain symptoms at 12 weeks from treatment initiation.

Using this baseline, shoe inserts significantly improved reported PF pain in the short term (<6 weeks, 24% absolute reduction in pain; 95% CI, 20–29), medium term (6–12 weeks, 15% reduction; 95% CI, 12–29), and long term (>12 weeks, 37% reduction; 95% CI, 32–49).

Cost analysis reveals no differences in effectiveness
Because of the large variety of designs of OTC-SI on the market—and the corresponding variety in costs—a study in 2007 evaluated different brands of OTC-SI. Thirty-five asymptomatic individuals were asked to ambulate a walkway 7 times, once with no shoe inserts and 6 more times with 6 different brands of OTC-SI. The authors used an in-shoe strain gauge to measure the pressure generated at the heel.

Though costs varied from $9 to $45, the average pressure during heel strike without an insert (mean 263 kPa) was significantly reduced by all OTC-SI tested (measuring 213–235 kPa). The authors concluded that cost played no role in the alleviation of forces exerted on the heel when wearing OTC-SI.

Clinical considerations
Despite discrepancies in the reported effectiveness of shoe inserts in the treatment of patients with PF pain, the relative low cost of OTC-SI may warrant their use in initial management. Furthermore, cost does not seem to be an effective indicator of an OTC-SI’s ability to reduce pressure generated during heel strike. Given the significant cost of CM-SI, and noting also the paucity of data supporting their use, it may be wise to consider other treatment modalities instead. It would be helpful to have well-done studies comparing shoe insert therapies with control groups.

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Cleveland Clinic
Cleveland, OH

REFERENCES
What is the best skin closure for a cesarean section?

**Bottom line**

Methods for cesarean skin closure include suture, staple, and tissue adhesive. Obstetric and general surgery studies have reached the following conclusions:

- **Sutures vs staples**: sutures result in a longer operating time, but less postoperative pain and a better cosmetic result.
- **Sutures vs tissue adhesive (the most commonly used is 2-octyl cyanoacrylate, Dermabond®)**: sutures result in a lower incidence of dehiscence.
- **Staples vs tissue adhesive**: staples are faster, but other outcomes are similar.

Staples need to be removed, unlike tissue adhesive and subcutaneous sutures. Surgeons and women should discuss current evidence in choosing how the skin will be closed.

**Evidence summary**

A Cochrane review of skin closure for cesarean delivery identified only 1 RCT comparing subcutaneous sutures with staples for cesarean skin closure in 50 patients.¹

This Cochrane review did not include tissue adhesive. Sutures took longer than staples to place (mean, 605 vs 47 s; *P*<.001), but women reported less pain at time of discharge (score on a 10-point pain scale: 5.1 vs 6.6; *P*<.003) and at a postoperative visit (score on the pain scale: 0.5 vs 2.0; *P*<.002). Cosmetic results with sutures were generally preferred by both patients (rated excellent 60% vs 36%, good 40% vs 48%, and fair 0% vs 4%; *P*=.04) and physicians (rated excellent 60% vs 24%, good 32% vs 48%, fair 8% vs 24%, and poor 0% vs 4%; *P*=.01).²

A separate Cochrane review (14 RCTs; 1,152 patients) addressed tissue adhesive for closure of surgical incisions, although without a focus on cesarean section closure.³ Using data from 5 studies (448 operations), sutures led to lower rates of wound dehiscence than tissue adhesive (RR=4.3; 95% CI, 1.4–13). Comparing sutures with tissue adhesives, time of operation results were conflicting and inconclusive; there was no difference in rates of infection or operator and patient satisfaction.³

The only RCT comparing staples with tissue adhesive involved closure of neck surgery incisions; this study found that staples (n=15) involved shorter operating time than tissue adhesive (n=14) (mean, 28 vs 95 s; *P*<.001), with comparable cosmetic result and surgeon and patient satisfaction.⁴ A 2010 RCT, published since the Cochrane review, comparing staple closure (n=38) with tissue adhesive (n=36) for elective hemicolecotomy, similarly found staples to be faster, but with no significant difference in cosmetic result and surgeon and patient satisfaction.⁵

**Need for further study**

More research is needed to document the risks and benefits of various methods of skin closure for cesarean sections. RCTs comparing tissue adhesive with suture and staples for cesarean skin closure would more directly determine the best method. Studies should look at closure not only under ideal conditions, but also in high-risk settings such as infection and tissue tension.

For now, providers can describe available evidence when helping women decide which method to use in what will be the most visible result of their delivery by cesarean.

Lee T. Dresang, MD
U of WI School of Medicine and Public Health
Madison, WI

**REFERENCES**

Is oral prednisone as effective as high-dose IV steroids as initial treatment in a patient with a COPD exacerbation?

Evidence-Based Answer

Yes. For the initial inpatient management of chronic obstructive pulmonary disease (COPD) exacerbations in noncritically ill patients, oral steroids are associated with similar outcomes as intravenous (IV) steroids. In addition, patients treated initially with oral steroids appear to have shorter hospital stays and lower hospital costs. (SOR: B, based on an RCT and a cohort study.)

In 2007, a double-blind RCT evaluated patients hospitalized for an acute COPD exacerbation. One group of 94 patients received a 5-day course of 60 mg oral prednisolone with an IV placebo, while 99 patients received 60 mg IV prednisolone and an oral placebo. The primary outcome included early (within 2 weeks) and late (2 weeks to 3 months) treatment failure defined as death, admission to intensive care unit, readmission within 90 days, or intensified treatment with further steroids, antibiotics, or theophylline.¹

This was a noninferiority study design that used the lower bound of a one-sided 95% CI; a difference in the treatment failure rate of <15% would deem oral treatment not inferior to IV treatment.¹

The results revealed no difference in the overall treatment failure rate (61.7% vs 56.3%), IV-treated group vs oral-treated group; one-sided 95% CI lower bound for the difference, −5.8%), early failure rate (17.8% vs 18.4%, respectively; one-sided 95% CI lower bound for the difference, −9.4%), or late failure rate (54% vs 47%, respectively; one-sided 95% CI lower bound for the difference, −5.6%).¹

A recent large retrospective cohort study including 79,985 patients admitted with COPD exacerbation from 414 hospitals compared treatment failure rates in 73,765 (92%) patients initially treated with high-dose IV steroids (120–800 mg prednisolone equivalents per day on hospital day 1–2) versus 6,220 (8%) patients initially treated with low-dose oral steroids (20–80 mg prednisolone equivalents per day). Primary treatment failure was defined as initiation of mechanical ventilation after hospital day 2, death during hospitalization, or readmission for COPD within 30 days of discharge. Secondary measures included length of hospital stay and cost.²

A total of 1.4% (95% CI, 1.3%–1.5%) of patients initially treated with IV steroids died, compared with 1.0% (95% CI, 0.7%–1.2%) of patients initially treated with oral steroids. A total of 10.9% of IV-treated patients had treatment failure (95% CI, 10.7%–11.1%), compared with 10.3% of oral-treated patients (95% CI, 9.5%–11.0%).²

A multivariable analysis was conducted to create a propensity-matched cohort (matched for comorbidities and multiple measures of severity), which paired a patient in the oral therapy group with a similar patient in the IV treatment group. This analysis revealed patients treated with oral steroids had a lower risk of treatment failure (OR 0.84; 95% CI, 0.75–0.95), shorter length of stay (OR 0.90; 95% CI, 0.88–0.91), and lower hospital costs (OR 0.91; 95% CI, 0.89–0.93). In models adjusting for patient, hospital, and physician characteristics and controlling for the early use of other treatments and diagnostic tests, the risk of treatment failure with oral treatment was not significantly different from that with IV treatment (OR 0.93; 95% CI, 0.84–1.02). But patients treated with the oral regimen again had a shorter length of stay (OR 0.92; 95% CI, 0.91–0.94) and lower costs (OR 0.93; 95% CI, 0.91–0.94).²

A 2007 evidence-based guideline by a collaborative working group (that was published before the above studies) states that oral or IV glucocorticosteroids are recommended for hospital management of an acute exacerbation of COPD (based on multiple RCTs with consistent findings) and that the exact doses are unknown, but an overall recommendation of 30 to 40 mg oral prednisolone daily for 7 to 10 days was a reasonable compromise between efficacy and safety (based on nonrandomized trials and observational studies).³

John Paul Armilio, MD
Corey Lyon, DO
Research FMR
Kansas City, MO


What is the best imaging modality for the diagnosis of gallbladder carcinoma?

Evidence-Based Answer
Transabdominal ultrasound is the first-line imaging modality to detect clinically suspected gallbladder carcinoma, although estimates of sensitivity vary widely (25%–85%). (SOR: B, based on retrospective cohort studies.) Endoscopic ultrasonography, thin-slice computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP) can further detail the extent of primary gallbladder carcinoma. (SOR: C, based on expert opinion.)

In the United States, the annual incidence of primary gallbladder carcinoma is 1 to 2.5 per 100,000, while in Japan it is 7 per 100,000. China has had an increasing rate of gallbladder cancer in the past few decades.1

A retrospective US cohort study covering 28 years included 40 patients with proven primary gallbladder carcinoma. Twenty-two of those 40 patients received ultrasounds. Gallbladder masses were found in 11 of those 22 patients (50% sensitivity). CT evaluation had a sensitivity of 40%.2 Another retrospective US cohort study found that 22 of 26 patients with primary gallbladder carcinoma had masses on preoperative ultrasound (85% sensitivity).3

A Japanese retrospective study with 51 patients with known gallbladder cancer reviewed ultrasounds received by 25 of those patients. Nine of the 25 showed the malignancy (36% sensitivity). Only 10 patients with primary gallbladder carcinoma underwent CT, but 7 of those 10 studies revealed the cancer (70% sensitivity).4

In China, a retrospective study of the 199 patients with primary gallbladder carcinoma (between 1985 and 1998) found that only a small percentage of these patients were diagnosed at an early stage (28 of 199 patients). Of those 28 diagnosed at an early stage, only 7 were diagnosed preoperatively by ultrasound, ultrasound plus CT, or endoscopic retrograde choledochopancreatography (25% sensitivity). Ultrasound sensitivity was reduced by thick abdominal walls and overlying bowel gas patterns in this group.5

According to a 2008 Japanese narrative review article, diagnosis of primary gallbladder carcinoma can be approached in a stepwise fashion. The authors asserted that 50% of gallbladder carcinomas are found as tumors on abdominal ultrasound; ultrasound is inexpensive, noninvasive, and widely available; and further investigation to localize the lesion and to assess the degree of extension includes endoscopic ultrasonography, thin-slice CT, MRI, and MRCP.6

What is the most effective treatment for insomnia in the elderly?

Evidence-Based Answer
Cognitive behavioral therapy (CBT) improves certain sleep parameters and should be considered first-line therapy for elderly patients. (SOR: A, based on a systematic review.) Pharmacologic therapy should aim to match the patient’s symptoms with the properties of the drug, with preference given to short- to intermediate-acting benzodiazepine receptor agonists or ramelteon. (SOR: C, based on expert opinion.) Over-the-counter and prescription antihistamines are generally inappropriate for use in the elderly due to adverse effects. (SOR: C, based on expert opinion.)

A Cochrane review of CBT for sleep included 6 RCTs with 282 adults older than 60 years.1 Studies varied in the frequency and specific CBT interventions used. Immediately after treatment, CBT demonstrated improvements compared with baseline in total sleep duration (15 min longer; 95% CI, 7 to 36) and wake after sleep onset (22 min shorter; 95% CI, 6 to 37). Endpoints not achieving statistical significance were early morning wakening and sleep efficiency. After a year or more, a significant effect on wake after sleep onset
was no longer seen in the CBT group (13 min shorter; 95% CI, –3 to 29), while total sleep duration continued to improve (32 min longer; 95% CI, 8 to 71). CBT is not known to have any significant adverse effects.

Pharmacologic treatments currently approved by the US Food and Drug Administration include benzodiazepines hypnotics, nonbenzodiazepine hypnotics, and a melatonin receptor agonist. A meta-analysis of 24 RCTs (n=2,417) comparing short-term hypnotic use with placebo in persons aged 60 and older found that treatment with sedative hypnotics subjectively improved quality of sleep (effect size 0.14, P<.05). (An effect size of 0.2 is considered small, 0.6 moderate, and 1.2 large.) Improvements were seen in total sleep time (mean 25 min longer; P<.001) and number of night time awakenings (–0.63; P<.001). Cognitive adverse effects, however, were 4.8 times more common (95% CI, 1.5–15), and daytime fatigue was 3.8 times more common (95% CI, 1.9–7.8) with hypnotic use versus placebo.

A double-blind study evaluating the use of the melatonin receptor agonist ramelteon versus placebo in 693 elderly persons found ramelteon significantly improved sleep latency (–8.3 min at week 1; P=.008) with a low incidence of adverse effects and no rebound or withdrawal effects over 5 weeks of treatment.

Other classes of medications utilized off-label for elderly patients include antihistamines, antidepressants, antipsychotics, and anticonvulsants. Due to insufficient evidence for effectiveness and the potential for serious adverse effects, the use of antihistamines, antipsychotics, and anticonvulsants are not recommended for elderly patients. Antidepressants are recommended for use in persons with comorbid depression.

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The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Medical Department of the US Army or the US Army Service at large.

drugs and necrotizing fasciitis, causality has not been proven, and other factors, such as increased pain with necrotizing fasciitis more often requiring pain medication, could also explain such a relationship.

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What is the best way to diagnose compartment syndrome?

Evidence-Based Answer

Clinical examination is not a reliable way to diagnose acute compartment syndrome (ACS), although the absence of pain, paresis, and paresthesia certainly rules it out. (SOR: A, based on a meta-analysis.) As a practical matter, patients with injuries serious enough to develop ACS often cannot be examined adequately anyway. (SOR: B, based on a cohort study.) Measurement of differential pressure (denoted as ∆p, the diastolic blood pressure minus the absolute compartment pressure) with ∆p <30 mmHg is the gold standard for diagnosis of ACS. (SOR: C, based on expert opinion.) The absolute compartment pressure (ACP) is not a reliable substitute for ∆p. (SOR: B, based on a diagnostic cohort study.)

A meta-analysis of 4 cohort studies (n=132, mean age 36 years, 80% male) evaluated whether the clinical findings of pain at rest or with passive stretch, paresthesia, and paresis were useful for the diagnosis of impending ACS. For these clinical findings, the sensitivity was low (13%–19%) and the specificity was high (97%–98%), resulting in a positive predictive value of 11% to 15% and a negative predictive value of 98%. These authors concluded that the absence of these signs and symptoms were more useful for excluding the diagnosis than in establishing the diagnosis by their presence.1

A 6-month prospective observational cohort study evaluated a screening protocol to detect lower extremity ACS in patients (n=45, mean age 38 years, 76% male) admitted to a shock-trauma intensive care unit. Patients were screened on admission and every 4 hours for 48 hours. Physical examination included measurement of calf circumference (at 4 cm below the tibial tuberosity); calf pain at rest and with passive stretch; assessment of dorsal pedal and posterior tibial pulses; and neurological assessment of motor and sensory function. When the physical examination was suspicious or unreliable (altered mental status, sedation, paralysis, etc), measurements of anterior and posterior compartment pressures were performed. The ∆p <30 mmHg was considered diagnostic for ACS and prompted fasciotomy.2

ACS was identified in 9 of 45 patients (20%), with an average time to recognition of 9±5 hours and ∆p=20.6±3.7 mmHg at the time of diagnosis. In this cohort, leg circumference was unobtainable in 51% of patients because of dressings/splints and calf pain, and neurological assessment was unobtainable in 69% of patients because of sedation or neurologic status. These authors concluded that physical examination was unreliable for diagnosing ACS.2

A prospective study compared the effectiveness of using the ACP >30 mmHg versus the standard of ∆p <30 mmHg for the diagnosis of ACS in a cohort of 39 patients (mean age 34 years, 66% male) having 42 tibial diaphyseal fractures. Blood pressure and ACP were taken every half hour beginning an average of 2 hours after injury and continued for 72 hours. The mean ACP and the ∆p for the six 12-hour periods were calculated. A value of ∆p <30 mmHg over 2 consecutive half-hour periods was considered diagnostic of ACS and prompted fasciotomy.3

Over a 72-hour period, mean ACP readings ≥30 mmHg were documented in 33 patients, while only 3 had a ∆p <30 mmHg (and were treated by fasciotomy). All patients except 1 were followed for a mean of 36 months; all fractures healed and there were no sequelae of ACS. These authors concluded that ACP readings >30 mmHg were not reliable for the diagnosis of ACS.3

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What is the most effective treatment for community-acquired pneumonia in immunocompromised adults?

**Evidence-Based Answer**

Initial empiric dual-therapy with a β-lactam antibiotic and a macrolide decreases mortality in immunocompromised patients (IPs) with community-acquired pneumonia with bacteremia compared with monotherapy. (SOR: C, a secondary outcome in a retrospective cohort study.) If resistance due to beta-lactamase is a concern, a broader-spectrum antibiotic (eg, cefepime or imipenem) may be appropriate for IPs with known pneumococcemia. (SOR: C, extrapolated from a retrospective cohort study.)

A retrospective cohort study of 95 patients (49 men, 46 women, mean age 63 years) hospitalized with pneumonia and bacteremia evaluated the impact of initial dual-antibiotic therapy compared with monotherapy on mortality. Antibiotic therapy was initiated within 8 hours of admission. Forty-four percent (42/95) of patients received monotherapy (cefuroxime) and 56% (53/95) received dual therapy (46 patients received ceftriaxone plus macrolide and 7 patients received cefuroxime plus macrolide). Twenty-one percent (9/42) of patients in the monotherapy group were immunocompromised versus 17% of patients (9/53) in the dual-therapy group.¹

The monotherapy group had significantly higher mortality than the dual-therapy group (26% [11/42] vs 7.5% [4/53], respectively, \( P = .02 \)). An immunocompromised state did not significantly increase mortality risk (OR 0.38; 95% CI, 0.05–2.9).¹

A retrospective analysis compared 69 hospitalized IPs (most with malignancies; mean age 64 years) with 191 hospitalized nonimmunocompromised patients (N-IPs; mean age 62 years). All had pneumococcemia, 84% from pneumonia. Patients with AIDS were intentionally excluded. IPs did not differ from N-IPs in the presence of fever, obtundation, type of lung involvement (multilobar pneumonia, pleural effusion), or frequency of primary bacteremia.²

Overall mortality was not statistically significantly greater in IPs than N-IPs (33% vs 23%; \( P = .07 \)). However, multilobar pneumonia specifically did have a higher mortality in IPs (OR 7.9; 95% CI, 4.1–15; \( P < .001 \)), and IPs with acute leukemia and lymphoma had a significantly greater mortality than N-IPs (54% related mortality; \( P = .05 \)). In addition, septic shock was significantly more frequent in IPs than N-IPs (28% vs 14%; \( P = .01 \)). In considering therapy, penicillin resistance or moderate penicillin susceptibility was more frequent in isolates from IPs than N-IPs (38% vs 20%; \( P = .009 \)).²

Given these clinical features, these authors recommended broad-spectrum antibiotics (eg, cefepime or imipenem) as first-line antibiotics for immunocompromised and neutropenic patients who develop pneumococcemia.²

Consensus guidelines recommend using either a β-lactam (ceftriaxone, cefotaxime, or ampicillin-sulbactam) plus a macrolide (azithromycin or clarithromycin) or a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin) for management of community-acquired pneumonia in outpatients or inpatients (non-ICU and ICU) with immunocompromising conditions, who are taking immunosuppressing drugs, are asplenic, or have a malignancy. For penicillin-allergic patients, a respiratory fluoroquinolone plus aztreonam is recommended.³

If *Pseudomonas* is a concern, one of several combination regimens is recommended: (i) an antipneumococcal, antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus antipneumococcal fluoroquinolone (ciprofloxacin or levofloxacin); (ii) previous β-lactam plus an aminoglycoside and azithromycin; or (iii) previous β-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone.³

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**References**


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We invite your questions and feedback. Email us at EBP@fpin.org.
Thyroid neoplasia

Definitions
- Adenoma
  - Benign thyroid tumor
- Carcinoma
  - Most common endocrine neoplasia
  - Types
    - Papillary
    - Medullary
    - Follicular
    - Anaplastic

Diagnostics
1. History
- Most patients with thyroid nodules asymptomatic
  - May complain of neck pressure or pain if spontaneous hemorrhage into nodule
- Radiation exposure (especially head/neck)
- Hoarseness
  - Vocal cord paralysis suggests malignancy
- Dysphagia
- Cough
- CNS disturbance
  - Heat intolerance
  - Irritability
  - Insomnia
- Frequent bowel movements
- Weight loss
- Infertility
- Dyspnea (advanced disease)
- Family history of thyroid disease

2. Physical exam
- Painless thyroid nodule
- Thyroid mass
  - May be nodular, hard, or fixed
- Cervical lymphadenopathy
  - Worse prognosis
- Possible malignancy
  - Vocal cord paralysis
  - Lateral cervical lymphadenopathy
  - Fixation of nodule to surrounding tissues

3. Diagnostic testing
- Malignancy of nodules
  - Nonpalpable nodules have same risk of malignancy as palpable nodules of same size
  - Evaluate all nodules ≥1 cm unless risk factors present
  - Incidental nodules found by FDG-PET for other reasons have a 33% chance of malignancy; evaluate regardless of size
- CT/MRI
  - Not routinely used
  - Rarely diagnostic for malignant lesions in nodular thyroid
  - Can be useful for suspected substernal extension of goiter
  - CT contrast medium contains iodine and reduces uptake of radioisotope
- Calcitonin assay
  - Serum marker for medullary thyroid carcinoma (MTC)
  - Increased in renal impairment and in patients taking proton pump inhibitors
  - A must if family history of MTC or multiple endocrine neoplasia type 2
  - 10–100 pg/mL is abnormal
  - >100 pg/mL highly suggestive of MTC
- Thyroid peroxidase
  - High levels in presence of diffusely enlarged thyroid suggestive of autoimmune or Hashimoto’s thyroiditis
- Thyroglobulin assay
  - Not useful in the work-up of thyroid nodules

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To review complete topic monograph visit www.fpin.org/page/ebpemedref
**H₂ blockers are as effective as PPIs for long-term relief of nonulcer dyspepsia**

**Bottom line**
H₂ blockers are as effective as proton pump inhibitors (PPIs) for long-term relief of nonulcer dyspepsia and for preventing relapse of symptoms. (SOR: A, based on multiple meta-analyses.)

**Evidence summary**
A 2006 Cochrane review compared RCTs that evaluated antacids, H₂ blockers, PPIs, prokinetics, mucosal protecting agents, and antimuscarinic agents against each other or placebo for the treatment of dyspepsia. Participants had to be adult patients with negative or insignificant findings on endoscopy or barium studies. Additionally, trials whose participants had predominantly reflux or heartburn symptoms were excluded.¹

In 12 RCTs evaluating H₂ blockers against placebo (n=2,183), the relative risk reduction (RRR) for dyspepsia symptoms was 23% (95% CI, 8%–35%; NNT=7). In 10 trials evaluating PPIs against placebo (n=3,347), the RRR was 13% (95% CI, 4%–20%; NNT=10).¹

Only 1 RCT (n=558) compared H₂ blockers with PPI therapy. Using the outcome of symptom cure, no significant difference was noted between the 2 medications (RRR for PPI vs H₂ blocker 7%; 95% CI, –3 to 16).¹ An analysis of cumulative adverse events was not included.¹

A 2002 systematic review examined 6 RCTs (n=2,368) comparing PPIs with placebo, and 1 RCT (n=589) comparing PPIs with H₂ blockers in adults with nonulcer dyspepsia. Three were published studies and 3 were abstracts. Studies in which patients had biliary tract or gastroesophageal reflux disease, gastroparesis, lactose intolerance, malabsorption, parasitic infections, or previous eradication therapy for Helicobacter pylori were excluded.²

PPIs were found to be more effective than placebo in achieving an excellent or good outcome, defined as complete relief or mild symptoms, respectively (OR 1.81; 95% CI, 1.49–2.2; NNT=10). The comparison study with H₂ blockers showed no difference in long-term symptom relief (OR 1.38; 95% CI, 0.92–2.01).²

A recent double-blind RCT included patients presenting with new-onset dyspepsia defined as epigastric pain that could be accompanied with symptoms such as regurgitation, heartburn, nausea, or bloating. Patients were treated with antacids, H₂ blockers then PPIs at 1-month intervals, or PPIs first then H₂ blockers. This trial did not use a scale for symptom severity, but rather featured a dichotomous outcome—either the patient had “treatment success” or not. There was no statistically significant improvement in symptoms with a PPI start compared with an H₂-blocker start.³

**REFERENCES**


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1. A noncritically ill 50-year-old man with controlled hypertension presents to the emergency department with an acute exacerbation of chronic obstructive pulmonary disease (COPD). Along with other standard treatment for COPD exacerbation, a reasonable choice for the initial dose, frequency, and route of steroid would be:
   - a. Prednisone 20–80 mg orally daily
   - b. Prednisone 80–120 mg orally 3 times a day
   - c. Methylprednisolone 40 mg IV daily
   - d. Methylprednisolone 250 mg IV every 6 hours

2. Which of the following statements is true regarding group B Streptococcus (GBS) screening and management?
   - a. Current recommendations are to obtain vaginal-rectal cultures at 34 weeks' gestation
   - b. Clindamycin is the medication of choice for GBS prophylaxis in most patients
   - c. 10^4 colony-forming units per milliliter of urine is a positive screen for GBS bacteriuria
   - d. The incidence of early-onset group B streptococcal disease has not significantly changed in 20 years

3. Consistent evidence exists for the use of which type of shoe insert in the treatment of patients with plantar fasciitis pain?
   - a. Over-the-counter shoe inserts
   - b. Custom-made shoe inserts
   - c. Gel-foam heel cup orthoses
   - d. None of the above

4. Which of the following statements is true of skin closure with sutures for cesarean delivery?
   - a. It is faster than skin closure with staples
   - b. It is more likely to lead to wound dehiscence than closure with tissue adhesive
   - c. It results in less postoperative pain than closure with staples
   - d. It is more likely to result in an unfavorable cosmetic result than closure with staples

5. Ultrasound is the first-line imaging modality to detect primary gallbladder carcinoma because it is
   - a. Widely available, relatively inexpensive, and noninvasive
   - b. Consistently more than 90% sensitive
   - c. The most specific imaging modality
   - d. All of the above

6. Reasonable empiric antibiotic therapy for community-acquired pneumonia pending results of blood cultures for a 64-year-old man with a history of lung cancer with chemotherapy and radiation therapy in the past year would be:
   - a. Ampicillin-sulbactam 2 g every 6 hours and moxifloxacin 400 mg daily
   - b. Cefotaxime 1 g IV every 6 hours and clarithromycin 500 mg every 12 hours
   - c. Ceftriaxone 1 g every 12 hours and azithromycin 500 mg daily
   - d. Any of the above

7. Which statement is true about the use of anti-inflammatory medications for cellulitis?
   - a. Ibuprofen added to antibiotic therapy alleviates the need for hospitalization
   - b. Anti-inflammatory medications are contraindicated when patients have infections
   - c. Prednisolone may reduce the length of hospital stay when added to antibiotics to treat cellulitis
   - d. None of the above

8. For nonulcer dyspepsia:
   - a. H2 blockers are as effective as proton pump inhibitors (PPIs) for long-term symptom control
   - b. PPIs are more effective than H2 blockers for prevention of relapse
   - c. Patients report significantly better improvement starting therapy with a PPI
   - d. Patients report significantly better improvement starting therapy with an H2 blocker

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