In the second RCT, 124 adult patients with POD were randomized to pimecrolimus 1% twice daily for 1 month or placebo.\(^3\) After treatment, the pimecrolimus group had an average PODSI score of 2.6 versus 3.5 for the placebo group (between-group difference 0.9; 95% CI, 0.4–1.4; \(P=.001\)). The subgroup of patients (n=35) with topical corticosteroid-associated POD had a mean PODSI score of 5.4 at baseline and 2.3 on day 29 with pimecrolimus. Patients with steroid-associated POD receiving placebo had a PODSI score of 5.4 at baseline and 4.2 on day 29 (between-group difference 1.9; 95% CI, 0.6–3.1; \(P=.007\)).

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What is the optimum frequency for corticosteroid injections of the knee?

**Evidence-Based Answer**  
The evidence is limited on the optimum frequency of intra-articular corticosteroid (ICS) injections of the knee for treatment of osteoarthritis (OA). Current guidelines recommend ICS injections be performed no more frequently than every 3 months (SOR: C, expert opinion).

A randomized, double-blind, placebo-controlled trial of 66 patients between 40 and 80 years of age with radiologic evidence of OA compared the efficacy (pain) and safety (joint space width) of a scheduled ICS injection with placebo.\(^1\) The ICS group received injections (triamcinolone acetonide, 1 cc of 40 mg/mL) every 3 months over the course of 2 years while the placebo group received saline injections over the same period. Outcomes measured were improvement in subjective pain indices as well as joint space width (JSW) on X-ray.

The radiologic evaluation of JSW performed at study entry (ICS 4.1 mm vs placebo 3.9 mm), year 1 (ICS 4.0 mm vs placebo 3.9 mm), and year 2 (ICS 4.0 mm vs placebo 3.9 mm), revealed no significant differences between treatment groups and no signs of disease progression. At 1 year, the ICS group had significant improvement in range of motion (ICS 4.4° vs placebo 2.7°; \(P<.05\)). At 2 years the area under the curve analysis for differences in scores on the WOMAC VA 3.0 (visual analog scale, measuring 0–100, with 0 being no pain or stiffness) from baseline to month 24 showed significant differences between groups favoring ICS for night pain (ICS –0.66 vs –0.31 placebo; \(P=.0047\)) and joint stiffness (ICS –0.636 vs –0.320 placebo; \(P=.05\)).\(^1\)

A retrospective cohort analysis over a 20-year period studied 65 patients (35 rheumatoid arthritis and 30 OA) receiving ICS injections of varying frequency (interval not less than every 4 weeks) over a period of 4 to 15 years.\(^2\) The total injection count varied from 15 injections in 4 years to 167 injections over 12 years. Post hoc radiographs compared with earlier films did not reveal any correlation between frequency or total injection count and joint deterioration.

A consensus guideline from the American College of Rheumatology states that ICS injections should be given no more than every 3 months per joint for a maximum of 4 per year.\(^3\) This recommendation is based on concerns for steroid and crystal arthropathy, which have been variably reported in the human and animal literature.

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What is the utility of imaging studies in adult patients after a first-time seizure?

**Evidence-Based Answer**  
Neuroimaging with computed tomography (CT) is abnormal in up to half of unselected adult patients with a first-time seizure, resulting in a change in diagnosis in 44%, change in disposition in 26%, and change in acute management in 9%–17%. (SOR: B, systematic reviews of cohorts studies).

An American Academy of Neurology (AAN) subcommittee conducted a systematic review to examine the effects of neuroimaging on the management of the adult emergency patient presenting with a first-time seizure.\(^1\) The authors searched for English-language
studies evaluating patients with a first seizure and found 5 cohort studies with 1,672 patients. Although the studies included mostly adults, 3 included patients as young as 16 years, 1 included patients as young as 15, and the final study included some patients as young as 6 with afebrile seizures.

Up to 56% of patients had abnormal CT scans and in 9% to 17% the scans resulted in changes in acute management after finding traumatic brain injury, subdural hematomas, nontraumatic bleeding, cerebral vascular accidents, tumors, or brain abscesses.¹

The Guidelines in Emergency Medicine Network from the United Kingdom completed a systematic review to support a guideline on the management of adults with a first seizure in the emergency department.² The guideline working group searched multiple databases for studies on an unselected population of adults (≥16 years) presenting with a first generalized seizure.

Seven cohort studies showed 12% to 41% of adults with their first seizure had an abnormal head CT.² The authors reported data on the implications of abnormal neuroimaging from a single prospective study showing that abnormal head CT changed diagnosis in 44% of patients and changed disposition in 26% of patients with a first seizure. The specific changes in disposition were not delineated. The guideline did not comment on the size or quality of the included studies or the types of CT abnormalities found.

Another systematic review to support a practice guideline investigated only unprovoked first-time seizures in adults.³ The Quality Standards Subcommittee of the AAN searched multiple databases for studies of adults who had returned to their baseline level of function after a first seizure that was not secondary to cerebral trauma or stroke. Seven cohort studies (1,092 patients) reported significantly abnormal head CT scans in 1% to 47% (average 10%) of adults with an unprovoked first seizure. All of the significant abnormalities were reported to affect management through new diagnosis of brain tumors, vascular lesions, or cerebral cysticercosis.

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What are the indications for lumbar puncture in patients with acute headache?

**Evidence-Based Answer**

Acute headaches warrant further evaluation with lumbar puncture if there is suspicion for infectious meningitis or encephalitis, subarachnoid hemorrhage (SAH), or idiopathic intracranial hypertension (pseudotumor cerebri) (SOR: C, expert consensus opinion).

The decision to perform a lumbar puncture in the setting of an acute headache depends on the differential diagnosis and clinical presentation. A retrospective study spanning 27 years evaluated 445 adults treated for 493 episodes of acute bacterial meningitis.¹ Ninety-five percent of patients presented with fever, 88% with neck stiffness, 88% with altered mental status, and 11% with a petechial rash. Eighty-seven percent of patients had organisms identified by various culture methods. Seventy-five percent of cases had positive cerebrospinal fluid (CSF) culture.

A multicenter prospective cohort study enrolled 592 patients presenting with acute nontraumatic headache to evaluate the accuracy of ruling out a SAH with a negative head CT followed by a negative lumbar puncture (defined as no blood in the last tube collected).² A CT was performed within 12 hours of headache onset and if the CT was negative, a lumbar puncture was performed. Sixty-one cases of SAH were ultimately identified. Compared with CT with subarachnoid blood seen, xanthochromia in CSF, cerebral angiography, and autopsy (combined as a gold standard), the diagnosis strategy of head CT, followed by lumbar puncture if the head CT was negative for SAH had a sensitivity of 100% and a specificity of 67%, with a negative likelihood ratio (LR–) of 0 and a positive likelihood (LR+) ratio of 3.0.

Idiopathic intracranial hypertension (IIH) may present with headache, pulsatile intracranial noises, diplopia, papilledema, and possibly cranial nerve VI (abducens) palsy. A retrospective study (n=190) analyzed the opening pressures in subjects with acute IIH (n=116), chronic IIH (n=18), and neurologically healthy obese and nonobese patients (n=56).³ All opening pressures were obtained with patients in the lateral decubitus position with legs extended. In acute IIH the mean opening pressure was 344 mm H₂O (range 200–550 mm H₂O) and 90% of patients had an

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