

Episode 194 Subarachnoid Hemorrhage Recognition, Work-up, Diagnosis

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Traumatic vs atraumatic/spontaneous subarachnoid hemorrhage

The most common cause of SAH is head trauma. Trauma can cause SAH, but SAH can also cause trauma (ie. SAH causes syncope and patient falls or crashes their car, etc). Etiology (traumatic or atraumatic) dictates the workup and management.

	Traumatic SAH	Atraumatic SAH
Etiology	Most common cause of SAH. Occurs in 30-60% of patients with moderate to severe TBI.	85% due to aneurysm rupture. Less common causes include: vascular malformations, arterial dissection, amyloid angiopathy, RCVS, CVST, meningitis, (rarely) cerebral vasculitis.
Historical features	Mechanical fall/ traumatic injury followed by a headache/ LOC/ AMS.	Headache preceding syncope/LOC/ fall/ injury.
Imaging features (location of SAH)	Traumatic SAH = shearing of small vessels in subarachnoid space. Blood in the PERIPHERY of the brain (ie. sulci at edges of the cerebral hemispheres). Trauma can cause deeper structure SAH, but less common.	Blood in the DEEPER structures where aneurysms tend to be: around CSF cisterns near brainstem and circle of Willis.
Treatment	If no vascular lesion on CTA, NSx likely to recommend observation with repeat plain head CT in 24 hrs.	If vascular lesion (ie. aneurysm) on CTA thought to be the cause of SAH, NSx likely to consider intervention like endovascular coiling or neurosurgical clipping.
	CTA can miss aneurysms <3mm in size. For SAH in deeper structures where no aneurysm is identified, consider DSA (catheter-directed digital subtraction angiography) to pick up smaller aneurysms.	

Spontaneous subarachnoid hemorrhage is missed up to 7% of the time – why?

In 73% of cases of missed spontaneous SAH, the most common mistake was not considering the diagnosis and not ordering a non-contrast CT head (NCCTH). Spontaneous SAH has a spectrum of disease presentation. We can't rely on the "classic presentation" as our only trigger for ordering imaging. We also have to understand the limitations of NCCTH and pursue additional follow-up testing when appropriate (ie. LP and/or CTA). More on work-up below.

"Thunderclap" headache – is it accurate for subarachnoid hemorrhage diagnosis?

"Thunderclap" headache can mean different things to different people. In the <u>Ottawa SAH Rule for headache evaluation</u>, "thunderclap" headache is defined as abrupt onset severe headache that peaks instantly at onset. While most patients with SAH experience headaches that peak in far less than 1 hour, in order to capture all patients with SAH we should still be concerned about SAH in patients with a severe headache peaking up to 1 hour after onset. When patients experience a sentinel bleed and then a rebleed, you may elicit a story of a sudden severe headache that plateaued then suddenly got worse, this is also a concerning story requiring investigation for SAH.

To clarify the headache onset history with patients, consider asking:

- When did you first notice the headache?
- What were you doing at that time?
- How severe was it when you first noticed it on a scale of 0-10?
- Did it progress or get worse after that?
- When did the headache reach maximal intensity?

Differential diagnosis for "thunderclap" headache

*some of these diagnoses typically present with gradual onset, such as meningitis, however some patients with meningitis describe an abrupt onset

Common causes	Less common causes
RCVS (reversible cerebral vasoconstriction syndrome) – can be present alone or can coincide with SAH. Consider if lobar hemorrhage/vasogenic edema/infarct on plain CT as well. CTA usually shows multifocal artery narrowing that is dynamic (ie. would not be present on follow-up repeat CTA), commonly missed on initial imaging.	CVST (cerebral venous sinus thrombosis) – need CT venogram to diagnose, think about this in patients with headache + PE risk factors.
ICH (intracerebral hemorrhage).	PRES/Acute Hypertensive Emergency (posterior reversible encephalopathy syndrome) – severely elevated BP is usually not subtle and reversibility of headache/aLOC with BP management is the major clue.
Carotid/Vertebral/Intracranial Artery Dissection – need CTA to diagnose.	Pituitary apoplexy – pituitary bleed often seen on CT alone, but may need MRI to confirm (Risk factors: HTN, pituitary mass, pregnancy, peripartum).
Infectious meningitis – need LP to diagnose, can be viral or bacterial.	AACG (acute angle closure glaucoma) – have a quick look at the patient's eye(s) for redness/pain/blurry vision/fixed pupil and consider IOP check if present.

For more on these and other red flag headaches, listen to EM Cases Episodes <u>161</u> *and* <u>181</u>.

Risk factors for subarachnoid hemorrhage

- Standard vascular risk factors: hypertension, smoking, age >50
- Personal history of cerebral aneurysm: especially if >5mm in size, any documented growth on serial imaging, and/or located in the posterior circulation vessels
- Genetic risk factors: family history of cerebral aneurysm or aneurysmal SAH, connective tissue diseases like Elhers-Danlos (less so Marfan Syndrome), autosomal dominant Polycystic Kidney Disease
- **High-risk substance use**: binge or chronic ETOH, sympathomimetic use (cocaine, methamphetamines)

Historical/physical exam features concerning for subarachnoid hemorrhage

There is no single feature on history/ exam with a very high positive likelihood ratio for SAH. Nonetheless, the following are quite strongly and reliably associated with SAH: age >40, neck stiffness or pain, onset of headache on exertion (including sexual activity), vomiting, witnessed loss of consciousness, and elevated BP >160/100.

Think about SAH in patients presenting with headache PLUS:

- Altered LOC (ie. persistent GCS <15)
- Seizure
- LOC/syncope
- Neck pain (unilateral)
- Focal neurological deficits
- Low grade fever (from meningeal irritation due to the subarachnoid blood)

Pitfall: assuming that a patient presenting with a headache does not have a SAH if a fever is present is a common pitfall; a low grade fever is not uncommon with SAH due to meningeal irritation of blood In patients with SAH, the following historical features may be present (Carpenter et al. 2016; Perry et al. 2010; Perry et al. 2013; Perry et al. 2017):

- "Thunderclap" headache 83% of patients with SAH
- "Worst headache of life" ie. severe instantly peaking headache 95% of patients with SAH
 - This feature has poor interrater reliability
 - 70% of patients presenting to the ED with headache but *without* SAH will also endorse having "worst headache of life."
 - $\circ~$ Headache taking more than 1 hour to reach peak severity decreases the chance of patient having SAH, LR- 0.06

Pitfall: a common pitfall is assuming that "worst headache of life" alone is accurate for the diagnosis of SAH; 5% of patients with SAH will not describe the headache as the worst of their life, and there are many other morbid causes of headache that are patients describe as "worst headache of life".

- Neck stiffness 74% of patients with SAH
 - Subjective neck stiffness/ pain on history, LR+ 4.1
 - Objective neck stiffness on exam, LR+ 6.6
- Vomiting 62% of patients with SAH
- Loss of consciousness/ syncope 13% of patients with SAH

Pretest probability estimates of subarachnoid hemorrhage based on clinical features

ALL of the above features in isolation are more likely to be related to a non-SAH diagnosis than a SAH, but the following increases your pre-test probability of SAH to approximately 25%:

Instantly peaking severe headache (ie. "thunderclap") PLUS one of: neck stiffness, vomiting, OR loss of consciousness.

Patients with moderate to severe headache peaking within 1 hour with a normal neurological exam and none of the above features have a pre-test probability of SAH around 7%.

Previous headache history in assessing pretest probability of subarachnoid hemorrhage

We may be tempted to prematurely close and stop considering the diagnosis of SAH if a patient tells us they have had a prior similar headache. The evidence would suggest we need to take a more nuanced approach. A third to a half of patients with SAH have a sentinel bleed/headache that precedes the SAH. If a patient has had a similar headache in the recent past within 1 week to 1 month (some studies say up to 6 months), this should increase your pre-test probability for SAH. Conversely, if you have a patient with 3 or more similar headaches over more than 6 months, this should decrease your pre-test probability for SAH.

Pitfall: a common pitfall is ruling out SAH based on the historical feature of similar previous headache. A single similar previous headache within the last few months may represent a subarachnoid sentinel bleed and should increase your concern for SAH.

Physical exam for SAH

Screening neuro exam looking for stroke-like focal deficits

- o LOC
- Cranial nerves (esp. eyes)/ speech
- o Motor
- o Sensation
- o Coordination
- o Gait

Objective neck stiffness

o LR+ 6.6

Eye findings

- o Unequal pupils (ie. new anisocoria, herniation syndromes)
- Dysconjugate gaze (ie. CN 3, 4, or 6 palsy due to aneurysm mass effect). Not important to distinguish between CN palsies, but important to pick up abnormal pupils/ EOMs
 - CN 3 palsy dilated pupil, ptosis, eye "down and out"
 - CN 4 palsy eye "up and in" as eye moves medially
 - CN 6 palsy cross-eyed as eye moves laterally
- Subhyaloid hemorrhage on fundoscopy



Image credit: https://imagebank.asrs.org/file/1059/subhyaloid-hemorrhage

Pearl: the fundoscopic finding of subhyaloid hemorrhage in a patient presenting with abrupt onset headache is pathagnomonic for acute subarachnoid hemorrhage

Clinical decision rules for subarachnoid hemorrhage

The Ottawa SAH clinical decision rule can help decide which patients with headache require a work-up for SAH. The rule has a sensitivity of 100% and a specificity of 15%. It is important to carefully assess for inclusion and exclusion criteria for your patient.

The Ottawa Subarachnoid Hemorrhage Rule

Inclusion: Apply the rule for alert, GCS 15 patients \geq 15 years old who present with severe nontraumatic headache reaching maximum intensity within 1 hour. Headache onset within the last 14 days. **Exclusion:** Do NOT apply the rule for patients with new neurological deficits, previous aneurysms, previous SAH (subarachnoid hemorrhage), known brain tumors, or chronic recurrent headaches (\geq 3 headaches of the same character and intensity for >6 months).

Investigate for SAH if 1 or more high-risk variables present:

- 1. Age ≥40
- 2. Neck pain or stiffness
- 3. Witnessed loss of consciousness
- 4. Onset during exertion
- 5. Thunderclap headache (ie. instantly peaking pain)
- 6. Limited neck flexion on examination

Some considerations for using the Ottawa Subarachnoid Hemorrhage rule:

• Critiques of the rule include its low specificity and that this would lead to increasing usage of CT/ LP. Low specificity is the trade-off for a rule that is highly sensitive.

- Subsequent implementation study demonstrated that applying the rule does *not* increase CT use or LPs, and it may actually decrease CT utilization while increasing SAH pick-up rate.
- Interobserver assessments for the rule indicate moderate to substantial interobserver agreement in general for the rule; however, "worst headache of life" has poor interobserver agreement (kappa 0.45).
- The rule would suggest that, if applied correctly, SAH can be ruled out in patients who have no high-risk variables present.

Accuracy of non-contrast CT head for subarachnoid hemorrhage over time

The literature in this area has evolved. In 2011, Perry et al. found that noncontrast CT head (NCCTH) was likely over 90% sensitive for diagnosing SAH up to 24 hours from headache onset, but this decreases to 85% the next day and 50% after 1 week. Many studies now suggest 93-95% sensitivity between up to 12-24 hours; however, there is some variation in the literature about these numbers. For example, in 2016 Carpenter et al. published a meta-analysis that showed an overall sensitivity of 89% for NCCTH performed beyond 6 hours. On the flip side, a recent study from Vincent et al. in 2022 suggests that modern multi-slice NCCTH has a sensitivity of 99.3% up to 24 hours, however this is a retrospective singlecenter study.

The subarachnoid hemorrhage 6-hour rule for rule out with non-contrast CT

In 2011, Perry et al. published a landmark study that demonstrated NCCTH has a 100% sensitivity for identifying subarachnoid hemorrhage when performed within 6 hours of headache onset and when interpreted by an experienced radiologist. In their validation study in 2020, sensitivity of the 6-hour rule was found to be 95.5% due to 5 reported missed SAHs; however, only one of these was a true missed aneurysmal SAH. This case

was likely missed because the patient was severely anemic (63g/L) and CT scans are not reliable when differentiating blood from CSF at such low hemoglobin levels. Given that there was only one true missed SAH, the sensitivity of the 6-hour rule is likely around 98%.

Our experts recommend using the 6-hour rule to inform shared decisionmaking conversations with patients. Consider first whether you think your patient is at normal or extremely high-risk of SAH.

Normal risk	Extremely high-risk
If a normal risk patient has a negative NCCTH done within 6 hours of headache onset, the probability that they have a potentially life- threatening/ altering SAH is <1% and it is reasonable to stop the work-up here.	Think of extremely high-risk as the patient >50 years-old with severe, instantly peaking headache, neck pain, and a family history of SAH.
In rare cases, patients may wish to proceed with LP, in which case, consider a risk/ benefit discussion.	In these cases, Dr. Perry suggests doing an LP after negative NCCTH that was done within 6 hours of headache onset with the understanding that the probability these patients have a SAH is still likely <1%.

Pitfall: A pitfall that is often not considered is assuming that a non-contrast CT head done within 6 hours of headache rules out SAH in a patient with severe anemia. A certain degree of RBC concentration in the blood is required to appear on a CT. Don't rely on non-contrast CT head to rule out SAH (even within 6 hours of headache onset).

Pitfall: A common pitfalls is not considering alternate diagnoses of severe abrupt headache after the 6 hour rule has been applied and the patient has been ruled out for SAH. Don't forget the rest of the differential – even if you're done ruling out SAH after applying the 6-hour rule, continue your work-up if clinical concern remains for other diagnoses.

Likelihood of SAH in patients who present *after* 6 hours with a negative non-contrast CT:

After 6 hours, the sensitivity of NCCTH does decrease for picking up SAH (see above); however, if you assume a sensitivity of 89% from the 2016 Carpenter et al. meta-analysis, LR- 0.11, and a pre-test probability of 5.4% for the beyond 6-hour group, the post-test probability of SAH is 0.6% following a negative NCCTH. That means if you used NCCTH alone

beyond 6 hours, you would miss one SAH for every 166 patients worked up.

CT angiogram vs lumbar puncture after negative non-contrast CT in the workup of subarachnoid hemorrhage

Patients who may require further work-up after initial negative NCCTH:

- Extremely high-risk patients who had negative NCCTH performed within 6 hours of headache onset
- All patients with negative NCCTH performed more than 6 hours from headache onset

These patients can undergo CTA or LP for further investigation. Consider some of the pros and cons for CTA and LP: CTA:

- CTA will identify incidental aneurysms present in 2.5% of the population. If the aneurysm is less than 5mm, there is no good evidence to guide management. These incidental findings can lead to anxiety, decreased quality of life, insurability issues, and potentially risky and unnecessary surgical procedures. CTA may be the path of least resistance for emergency physicians because LPs take more time, but the harms from an incidental aneurysm finding can be significant.
 - If the aneurysm is greater than 5mm, we would need to LP anyway in the setting of a thunderclap headache to determine if it is acutely leaking
- Similar efficacy compared to LP for ruling out clinically important SAH
- Negative NCCTH + negative CTA = <1% post-test probability of SAH

- This sensitivity only applies if imaging is read by a qualified neuroradiologist
- CTA can miss small aneurysms less than 3 mm in size
- CTA can pick up alternative diagnoses that may present with thunderclap headache and may not be obvious on NCCTH
- CTA may not identify the diagnosis of SAH in cases of atraumatic non-aneurysmal SAH (up to 20% of cases)
- CTA increases total radiation exposure to the patient
- Small risk of anaphylaxis to CT contrast. Contrast dye allergy is a relative contraindication to CTA

LP:

- Up to 25% chance of post-LP headache, relatively easily treated with caffeine +/- blood patch
- Controversy exists over RBC cut-off and CSF interpretation
- Traumatic taps occur in 10-30% of LPs
- LP typically adds 2-4 hours to ED length of stay
- There are contraindications to LP like coagulopathy, anticoagulation, spinal hardware

In the episode, Dr. Perry and Dr. Lin describe their complimentary approaches to patients who require further work-up for SAH after negative NCCTH:

Dr. Perry's approach	Dr. Lin's approach		
Shared decision-making and risk/ benefit discussion with patients about different options.			
 LP should follow NCCTH when more investigations are needed (ie. extremely highrisk patient with negative NCCTH within 6 hours of headache onset or patient >6 hrs from headache onset after negative NCCTH) unless contraindicated or very delayed presentation (i.e., >1 wk). While 1/3 of LP have a traumatic tap, using RBCs <2000 x 10 6/L with no xanthochromia can be used to rule out SAH in all but extremely high-risk individuals. CTA is needed for patients where LP is contraindicated, presentation is delayed, NCCTH is positive for SAH or LP is positive. New 3rd nerve palsy (or partial palsy) with headache = enlarging PCOMM aneurysm until proven otherwise. Need CTA to assess, not LP 	 3-step approach: Is there a clear indication for CTA? Known aneurysm Focal neurological deficit (ie. uneven pupils, diplopia, motor/ speech) Unilateral acute neck pain/ trauma concerning for arterial dissection LP contraindication (ie. spinal hardware, anticoagulation, lab parameters) NCCTH positive for SAH (especially in unusual location, deep brain tissue or basal cisterns) Delayed presentation >1 week with concerning story Is there a clear indication for LP? Concern for infectious meningitis (ie. meningismus, low-grade fever, 		
(aneurysminas not bied yet).	 3. Grey-zone patients: Neither CTA or LP is clearly indicated. Engage patients in shared decision-making conversation. CTA: less invasive than LP, but may miss early meningitis (in forever mounted yet). Risk of picking up incidental aneurysm (present in 2.5% of the population) leading to possibly unnecessary procedures and affect ability to qualify for disability/life insurance going forward. May still need to do a follow-up LP if a small aneurysm is found on CTA. LP: more invasive than CTA and has associated procedural risks. Also risk of missing vascular causes of headache, but able to rule out early meningitis and won't pick up incidental aneurysm diagnoses. 		

CSF interpretation in subarachnoid hemorrhage

There is no good evidence to support waiting 12 hours before performing LP to increase the likelihood that xanthochromia will be present.

Xanthochromia:

- Yellowing of CSF due to presence of bilirubin from RBC breakdown
- Xanthochromia is present for at least 2 weeks, can take 2-12 hours to develop
- Different methods for measuring xanthochromia exist: visual inspection and various types of spectrophotometry (rarely available)
- Visual inspection for xanthochromia + RBC count performs better (100% sensitivity) than spectrophotometry alone

RBC count:

 In 2015, Perry et al. determined the optimal CSF RBC count cutoff value of 2000 x10⁶. When this RBC cut-off was combined with xanthochromia (ie. LP positive if either xanthochromia present or RBC count above of 2000 x10⁶), sensitivity was found to be 100% (CI 75-100%); however, this was based on a total of 15 established positive SAH cases. Given that SAH is rare after a negative NCCTH, this rule conservatively lowers post-LP odds of missed SAH to below 1 in 1000. Conversely, if LP is negative for xanthochromia and RBC count is less than 2000 x10⁶, our post-test probability of SAH is, conservatively, less than 1 in 1000 following negative NCCTH.

	LP results	Next steps
High-risk tap + negative NCCTH	RBC count >2000 x10 ⁶	СТА
-	AND/OR	
	Xanthochromia present	
Low-risk tap + negative NCCTH	RBC count <2000 x10 ⁶	Low/ normal-risk patient: Stop work- up for SAH
	AND	
		High-risk patient/ clinical concern for
	Xanthochromia absent	SAH remains: CTA

Pitfall: A common pitfall is ruling out SAH based on a CSF RBC count declining by 25% from tube 1 to 4. SAH can co-exist with traumatic tap, and this declining RBC count "rule" can be misleading.

Summary and key take-home points for subarachnoid hemorrhage diagnosis and workup

- The most common cause of SAH is head trauma. In atraumatic SAH, the most common cause is aneurysm rupture. On imaging, traumatic SAH usually shows blood in the periphery of the brain (sulci), and in aneurysmal atraumatic SAH usually the blood is in the deeper structures (basal cisterns).
- We miss the diagnosis of SAH mostly because we fail to consider it in the right patients and fail to order a non-contrast CT head.
- The Ottawa SAH rule and risk factors for aneurysm formation and rupture can help identify who needs a work-up.
- Remember that "thunderclap" headache has a differential diagnosis that includes more than just SAH (ie. cervical artery dissection, meningitis, CVST, etc).
- A prior similar headache within 1 month should raise your concern for SAH given the possibility of a sentinel bleed; however, 3 or more similar headaches over more than 6 months decreases the risk of SAH.

- Perform a screening neuro exam and look for speech/motor deficits and eye findings including anisocoria and gaze palsies.
 Objective neck stiffness has a high likelihood ratio for SAH.
- Except for extremely high-risk individuals, a non-contrast CT head performed within 6 hours of headache onset essentially rules out the diagnosis when interpreted by an experienced radiologist. In these extremely high-risk individuals, you could consider LP.
- Beware, non-contrast CT head will be unreliable for identifying SAH in severely anemic patients.
- Between 6 and 24 hours, plain CT is about 95% sensitive, so if you have very low pretest probability, this might be enough to rule out with shared decision making with the patient. Otherwise, consider further work-up.
- After 6 hours, if you've decided the patient needs further work-up after negative non-contrast CT head, LP is your go to test if there are no contraindications, the patient can tolerate the procedure, and SAH is your only worry. CTA would be acceptable too.
- Before ordering a CTA consider that 2.5% of the population has small asymptomatic aneurysms with very low risk of rupture and incidental aneurysm findings may lead to invasive procedures and harm.
- LP will help you identify infectious causes of headache like meningitis and non-aneurysmal causes of atraumatic SAH, while CTA will help you identify vascular causes of headache aside from SAH.
- An LP that is negative for xanthochromia and has fewer than 2000 x 10⁶/L RBCs should conservatively decrease the post-test probability of SAH to less than 1 in 1000 following a negative non-contrast CT head, which is low enough to rule out.
- A common pitfall is assuming a traumatic tap and no SAH if RBCs decline by 25% or more between tube 1 and tube 4. A traumatic tap *and* a SAH can co-exist.

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