CSF Bilirubin in Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) occurs most often due to the rupture of intracranial aneurysms that release blood into cerebral spinal fluid (CSF) and cause rapid increases in intracranial pressure. Testing is used to investigate the possibility of SAH in symptomatic individuals for whom computed tomography (CT) scan is unrevealing. A serum specimen for total bilirubin should be tested concurrently with the CSF specimen.

Disease Overview

Symptoms

- **Classic SAH:**
  - Individuals report worst headache ever experienced
  - May be accompanied by loss of consciousness, emesis, nuchal rigidity
- **Nonclassic SAH:**
  - Vague symptoms: headache, neck pain
  - Diagnostic challenge for clinicians
    - ~50% of patients present with minor bleed
    - ~30% of SAH is not correctly diagnosed
    - Outcome poor in this group

Diagnostic Issues

- CT is mainstay of diagnosis of SAH
  - Most sensitive if performed ≤12 hours after hemorrhage
  - Sensitivity rapidly decreases over time and may be negative in minor bleeds
- Spectrophotometric detection of bilirubin in CSF can be useful in patients with negative CT when SAH is still suspected

Physiology

- Red blood cells (RBCs) rapidly disseminate through the subarachnoid space following SAH
  - RBCs lyse and release intracellular oxyhemoglobin after dissemination
  - Oxyhemoglobin is metabolized to bilirubin in time-dependent fashion
  - Bilirubin imparts yellow tint (xanthochromia) to CSF
  - Blood in CSF from traumatic tap will not result in increased bilirubin in CSF

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity: ~87-93%
- Clinical specificity: 86-99%

Results

- **Positive**
  - Detection of bilirubin in CSF supports diagnosis of SAH if a suspicion for SAH is present
- **Negative**
  - Absence of red blood cells and bilirubin in CSF in conjunction with negative CT scan is sufficient to rule out SAH

Limitations

False negatives may occur:

- CSF specimens should not be collected <12 hours after suspected hemorrhage as bilirubin may not yet be detectable
- Exposure to light degrades bilirubin
• Traumatic tap may interfere with bilirubin measurements and may increase hemoglobin sufficiently so bilirubin is not detectable in CSF.