

Audit Template

Audit Title: A regional (Scotland) reaudit of CSF xanthochromia	
Lead Auditor: Dr Lindsay Graham	Audit date(s): March-June 2024
Please indicate if: Regional Audit Please indicate which hospital & location or region: Scotland	Report Author: Name: Dr Lindsay Graham Email: Lindsay.graham4@nhs.scot
Aims of the Audit: This audit consisted of two parts – a reaudit of the data provided in 2017 to see if the recommendations raised had been put into practice, and an audit of clinical data generated during a three month period of xanthochromia analysis. The latter half of the audit aimed to assess the utility of xanthochromia measurement in clinical decision making and alignment with the guideline NG228 (Subarachnoid haemorrhage caused by a ruptured aneurysm), published in November 2022.	

<p>Audit Method and Outcome(s): A survey form was circulated by e-mail to the Clinical Leads of service for each of the 14 Regional Health Boards in Scotland, as well as the local Scotland Audit Group (ACB) representatives. Completed survey forms were received by e-mail and data analysis performed using Microsoft Excel.</p> <p>Although not all health boards returned results of the audit, 9 responses were received and these included the largest health boards (NHSGGC and NHS Lothian). Responses were received from D&G, Fife, Forth Valley, GG&C, Grampian, Highlands, Lanarkshire, Lothian, and Tayside which covers a large proportion of the Scottish population. This is comparable to the previous audit in 2018 where 8 responses were received.</p> <p><u>Methodology questions</u></p> <p>Service provision</p> <p>7/8 laboratories provide a service for xanthochromia solely within working hours, with two extending out to 8pm. All labs provide some sort of weekend service, at a minimum Saturday am, with the majority providing service for the mornings of Sat/Sun. One laboratory provides a 24/7 service. Testing is centralised in all health boards with the exception of NHS Lothian, who provide testing on two sites. 6/8 services are UKAS accredited, 1 is unaccredited, and 1 is awaiting reaccreditation.</p>

Sample handling

Sample handling requirements are provided in the 'Revised National Guidelines for analysis of cerebrospinal fluid for bilirubin in suspected subarachnoid haemorrhage' (Cruickshank *et al.*, 2008). Compliance with these was audited in 2017 and the same questions were asked in the current audit. Results are shown below which show that there are now a higher number of laboratories which are compliant with the guidelines. Use of the pneumatic tube system is permitted in 3/9 health boards, however this is not a firm contraindication to xanthochromia analysis.

Criteria	2017	2024
Protect from light	6/8	9/9
Take simultaneous blood for bilirubin/protein	6/8	8/9
Avoid pneumatic tube system	4/8	6/9

Laboratory comments

All labs will add comments to the sample request if appropriate. Comments typically added are summarised below. All labs commented on samples which were not protected from light (in 2 cases it is unclear if this comment is returned to the user or simply recorded in the LIMS). All labs provided a comment to the user regarding the time requirement of >12 hours following sample collection. 8/9 labs commented on a bloodstained sample with an 'interpret with caution' comment (in 2 cases it is unclear if this comment is returned to the user or simply recorded in the LIMS).

Information recorded/ comment added if appropriate	No of labs
Sample not protected from light	9/9
Sample appearance – e.g. bloodstained	8/9
Results valid >12 hours after event/ >12 hours – 2 weeks or variant of the time requirement	9/9

Equipment and calibration

8/9 health boards use the Northstar Bio-UV spectrophotometer, with 1 using the Thermo Evolution 220 UV-visible spectrophotometer.

Most labs calibrate for wavelength and absorbance monthly, with one lab calibrating weekly and one calibrating 3 monthly. 8 of the labs use the calibration material recommended by Northstar (NIST Traceable holmium liquid wavelength standard and neutral density absorbance standard). The lab which uses Thermo instrumentation uses the Thermo Fisher Scientific Calibrated Validation Carousel which contains NIST traceable holmium perchlorate, hexane/toluene, potassium chloride and potassium dichromate. All labs perform calibration as per the automated software protocol.

Quality control

All labs run IQC samples as part of their xanthochromia analysis. The QC material used is listed below. It is clear that there is no standardisation of QC material which likely represents the lack of an appropriate commercial QC.

- In-house QC – using diluted Biorad Lyphocheck Diabetes Level 2 and Biorad Liquicheck Chemistry Level 2
- In-house QC - using diluted HbA1c and Technopath controls
- In-house QC – saline spiked with patient serum sample

- Sebia HbA1c IQC
- (3 labs) Technopath Multichem S Level 1 (dilutions from 1:20 - 1:50 in water)
- (3 labs) BioRad Multiquel IQC (dilutions from 1:20 - 1:50 in water)

Frequency	No of labs
Prior to each sample	3/9
Daily if a sample is received	4/9
3x per week	1/9
Weekly	1/9

The 2017 audit recommendation was that laboratories should run IQC material at a frequency appropriate to the service provided. The majority of labs run QC daily or prior to each sample received.

Clinical data

Number of samples

Most labs received between 20-45 samples over a 3 month time period, with an average (minus outliers) of 35 samples/3 months, which is approximately 12 samples/month. The two outliers were NHSGGC, with 72 samples, and NHS Lothian, with 212 samples (151 of these from RIE).

For 8/9 health boards, there were <5 inappropriate xanthochromia requests over a 3 month period (increased ICP, IIH, ?GBS, ?meningitis). At the RIE there were 64 inappropriate requests which if correct is hugely out of consensus with other labs).

CT scanning

Where data was available, the majority of samples put forward for xanthochromia analysis had a negative CT scan which was performed >6hours after the event. However in 10% (19/193) the CT scan was performed inappropriately early (<6 hours after the event). A small minority of samples (<5) were tested following a positive CT scan.

Testing outcomes

Outcomes were available for a total of 382 xanthochromia samples. Of the 382 samples. 91.9% (351/382) were negative, 5.2% (20/382) were inconclusive/equivocal and 2.9% (11/382) were positive. Of these positive samples, 3 previously had a positive CT. Final diagnosis of SAH within the population was 2.3% (9/382).

Audit Recommendations / Standards:

1. Improvement in sample handling/use of appropriate laboratory comments since 2017 audit
2. All labs now using IQC material – lack of standardisation is due to the unavailability of appropriate commercial QC.
3. Almost all labs (8/9) are using a Northstar Bio-UV spectrophotometer – is there a possibility for cross-lab standardisation?
4. The majority of xanthochromia requests are appropriate, however in ~10% samples the CT scan was performed inappropriately early – should labs consider a comment in this case? All labs comment that xanthochromia analysis should be performed >12 hours after symptom onset.
5. The diagnostic yield of xanthochromia analysis is low (2.3%) which is in agreement with other local/regional audits.

Please indicate to whom and when audit presented &/or circulated &/or published:

Poster presented at LabMed National Audit Day 2024

Audit recommendations / standards ratified by ... and when:

Date of audit report:

January 2025

Audit documents for upload to <http://www.acb.org.uk/whatwedo/science/audit.aspx>

Please include as attachments with this Audit Summary form if authors and the organising committee would like information to be publicly accessible on the ACB website Audit section.

Presentation

Standards/Recommendations

Blank Survey Questionnaire

Clinical Utility of Xanthochromia Analysis: Data from the Scottish National Audit

Dr Lindsay Graham, Blood Sciences, Ninewells Hospital, Dundee, DD1 9SY on behalf of the LabMed Scotland Audit Group

Introduction

Body text:

Cerebrospinal fluid (CSF) xanthochromia is a well-established laboratory test to aid in the diagnosis of subarachnoid haemorrhage (SAH) in patients with a negative computerised-tomography (CT) scan.

Xanthochromia is the yellowish appearance of CSF following bleeding into the subarachnoid space and is caused by the presence of bilirubin due to *in vivo* breakdown of blood, which occurs around 9-15 hours following a bleed. Measurement of xanthochromia by spectrophotometry at specific wavelengths can detect lower levels of bilirubin than can be observed visually.

It is recommended that a lumbar puncture is taken for xanthochromia analysis in patients who have a negative CT scan more than 6 hours after symptom onset. If the lumbar puncture (taken after >12 hours) is negative for xanthochromia, this acts as a 'rule-out' test for SAH with a high degree of certainty. This prevents progression to more invasive investigative procedures such as angiography.

In our laboratory (NHS Tayside) we receive several samples a week for xanthochromia analysis but very rarely report a positive sample. Xanthochromia samples are processed as a priority and therefore use a significant amount of laboratory resource. An audit was therefore proposed to the Scottish Audit Group to assess the appropriateness of xanthochromia requests and the prevalence of positive samples within various Scottish laboratories.

Method

A survey was distributed via email to all Scottish health boards in March 2024. Responses were received and collated in Microsoft Excel by a member of the Scottish Audit Group. Not all data was available for all health boards due to, for example, LIMS limitations, however the data received was similar across all regions. The data presented is therefore considered to be representative of xanthochromia analysis across Scotland.

Requesting and Imaging

CT imaging data was provided for 193 xanthochromia samples.

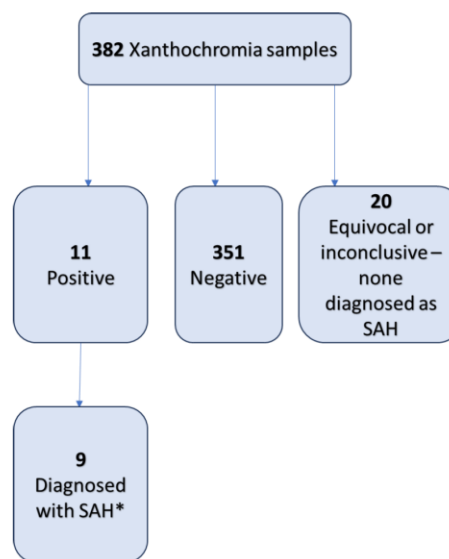
In these samples where data was available, 9.8% (19/193) were sent for xanthochromia analysis despite the CT scan being taken at <6 hours prior to analysis. NICE Guideline 228 (2022) states that if a CT head scan is negative within 6 hours of symptom onset, lumbar puncture is not required.

It is not known in these patients if other CSF tests were requested following lumbar puncture and the reason why xanthochromia analysis was requested in these cases.

3 patients underwent xanthochromia analysis despite having an initially positive CT scan.

Outcomes of xanthochromia analysis

Xanthochromia samples for which results outcomes were available are shown in the flowchart below.



Results outcome available for 382 samples tested across 3 months in 9 Scottish Health Boards.

- 351 (91.9% were negative)
- 20 (5.2%) were inconclusive or equivocal – reasons include large oxyhaemoglobin peak, tested too long after the event)
- 11 (2.9%) were positive
- 9 (2.3%) were diagnosed with SAH – one was reported as bloodstained (no final diagnosis) and one diagnosed with non-aneurysmal SAH.

Conclusions

In 9.8% of requests with CT data, a lumbar puncture was performed following a negative CT scan <6 hours after the event, despite this not being indicated. This may result in the patient undergoing a procedure unnecessarily.

Considering the results of analysis there were significantly more inconclusive/equivocal results (5.2%) than positive, which may cause diagnostic confusion. Only 2.3% of all xanthochromia samples yielded a positive result, with 2.1% leading to a subsequent diagnosis of SAH.

Xanthochromia analysis is a time-consuming practice for the laboratory with a low diagnostic yield. The utility of xanthochromia analysis compared to imaging methods in the diagnosis of SAH should be considered.

References

Best practice for sample handling and analysis taken from the Revised national guidelines for analysis of cerebrospinal fluid for bilirubin in suspected subarachnoid haemorrhage (Cruickshank et al. 2008)

Nice Guideline [NG228] Subarachnoid haemorrhage caused by a ruptured aneurysm: diagnosis and management.

Acknowledgements

- Members of the LabMed Scotland Audit Group.
- The Clinical Scientists and Trainees who completed the questionnaire for this Audit and provided data for their Health Board.