HDClarity

Site Assessment & Initiation

EHDN Biomarkers Meeting

London, 15 Jan 2016

CHDI
Accelerating therapeutic development for Huntington's disease

HUNTINGTON'S DISEASE CENTRE

UCL

Site Assessment

- The aim of site assessment is to assess the ability to conduct the study according to GCP and the HDClarity protocol
- Assessment will typically be conducted remotely using a site assessment questionnaire but may include a site visit if required
- The questionnaire will be completed by the site PI during a telephone meeting with HDClarity CC
- The CI will make recommendations to CHDI regarding the site's suitability to take part
- The site will be notified of the decision within 20 days of the meeting/visit

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Site Initiation

- The site initiation visit (SIV) can only occur after the site has an executed site agreement, completed regulatory requirements, obtained local ethics approval for the study and submitted all required documents to HDClarity CC
- Before the SIV, HDClarity CC will ensure that necessary site personnel, equipment and Clinical Site Study Binder, Training Videos, are available for the meeting, and that EDC logins have been activated
- The purpose of the SIV is to provide study specific training for site personnel and to ensure that the PI fully understands his/her responsibilities (21 CFR 312 Subpart D, ICH GCP Section 4)

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SIV Agenda

1. Study Overview (contact details, vendors, SAE/AE reporting)*
2. Protocol overview*
3. Roles, Responsibilities and Training*
4. Participant recruitment and follow-up
5. Lumbar puncture process
6. Biosample processing and shipment (HDClarity lab manual)
7. HDClarity eCRF
8. Source documentation and Clinical Study Site Binder
9. Monitoring
10. Site and participant payment
11. Facility Tour

*PI attendance required

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Site training

Clinical Study Site Training Materials:

1) Technical laboratory manual
2) Training video

Will be provided for and explained in detail during the SIV

These will give detailed information about:

- the HDClarity Study Biosamples Collection Kit contents
- research participant preparations for the lumbar puncture (LP), lidocaine injection and LP procedure
- CSF processing, blood collection, blood processing, cell count procedure
- packaging of samples and bar code reading.

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On-site training during the SIV

Practical on-site training:

How to identify the right lumbar vertebral interspace?

How to evaluate whether the first 1 ml of CSF is macroscopically bloody?

How to count leucocytes and erythrocytes?

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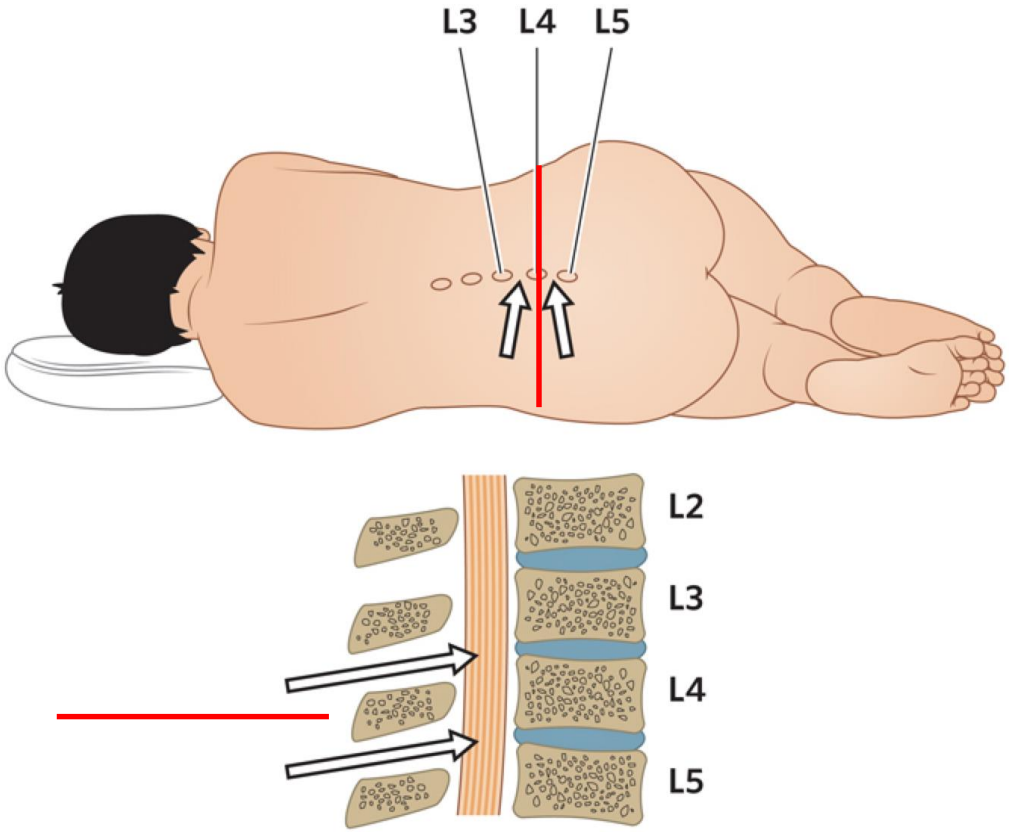
How to find the correct vertebral interspace

The line joining the most superior part of both iliac crests (Tuffier's line) crosses the spinous processs of L4



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Clinical Anatomy 12:43–54 (1999)

Detection of macroscopic blood contamination

Caveat:

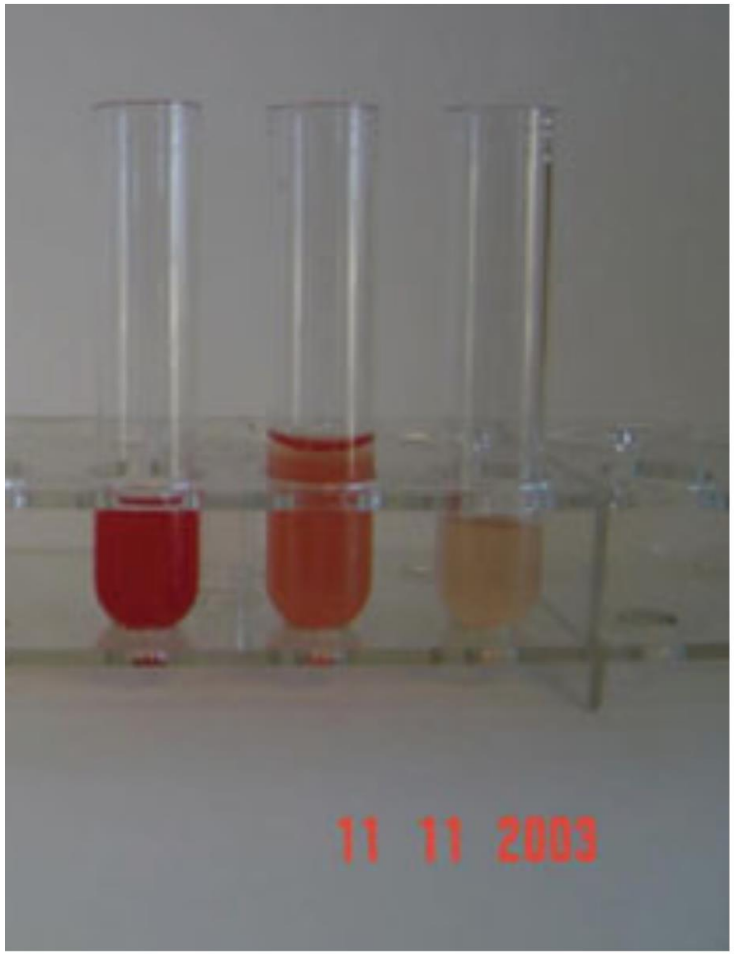
Detection limit of visual inspection of CSF for blood contamination is about 0.05 % vol/vol blood

(You et al., Proteomics 2005; 5(1):290–296)

Normal value blood:

ca. 5 Mio/µl

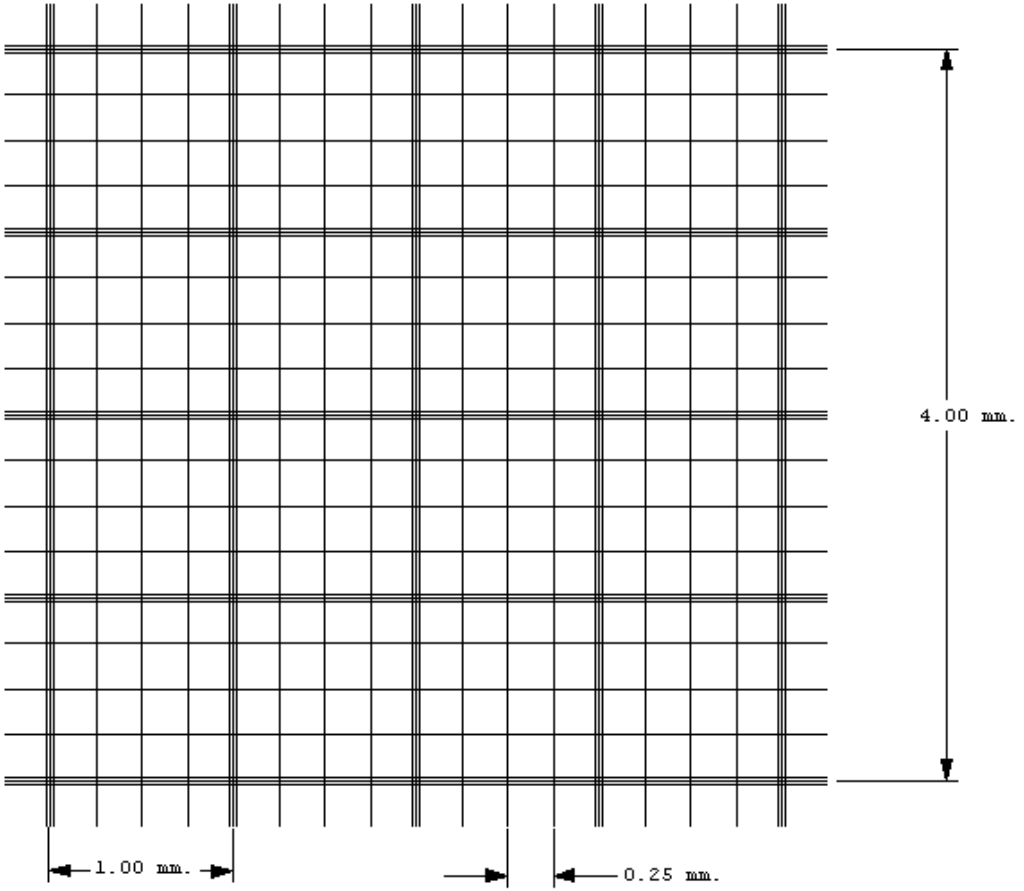
0.05%: 2,500/µl

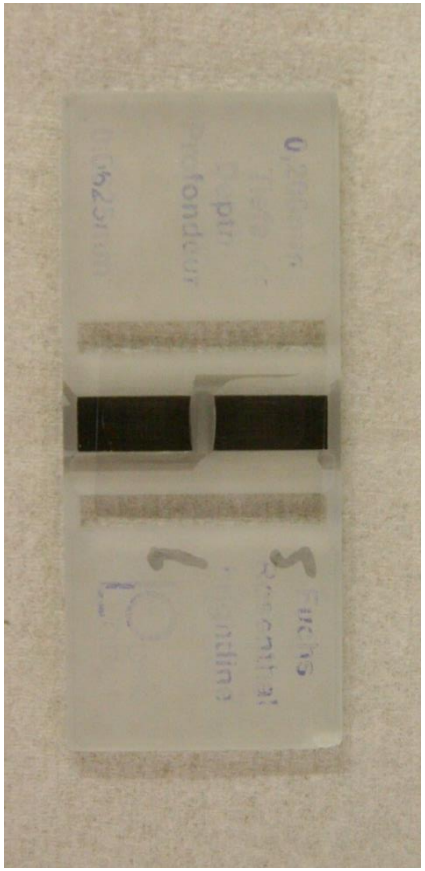


artificial bleeding

From: Cerebrospinal Fluid in Clinical Neurology, Deisenhammer et al. (eds) Springer 2015

Leucocyte and erythrocyte count





Fuchs-Rosenthal chamber, counting a 250x magnification

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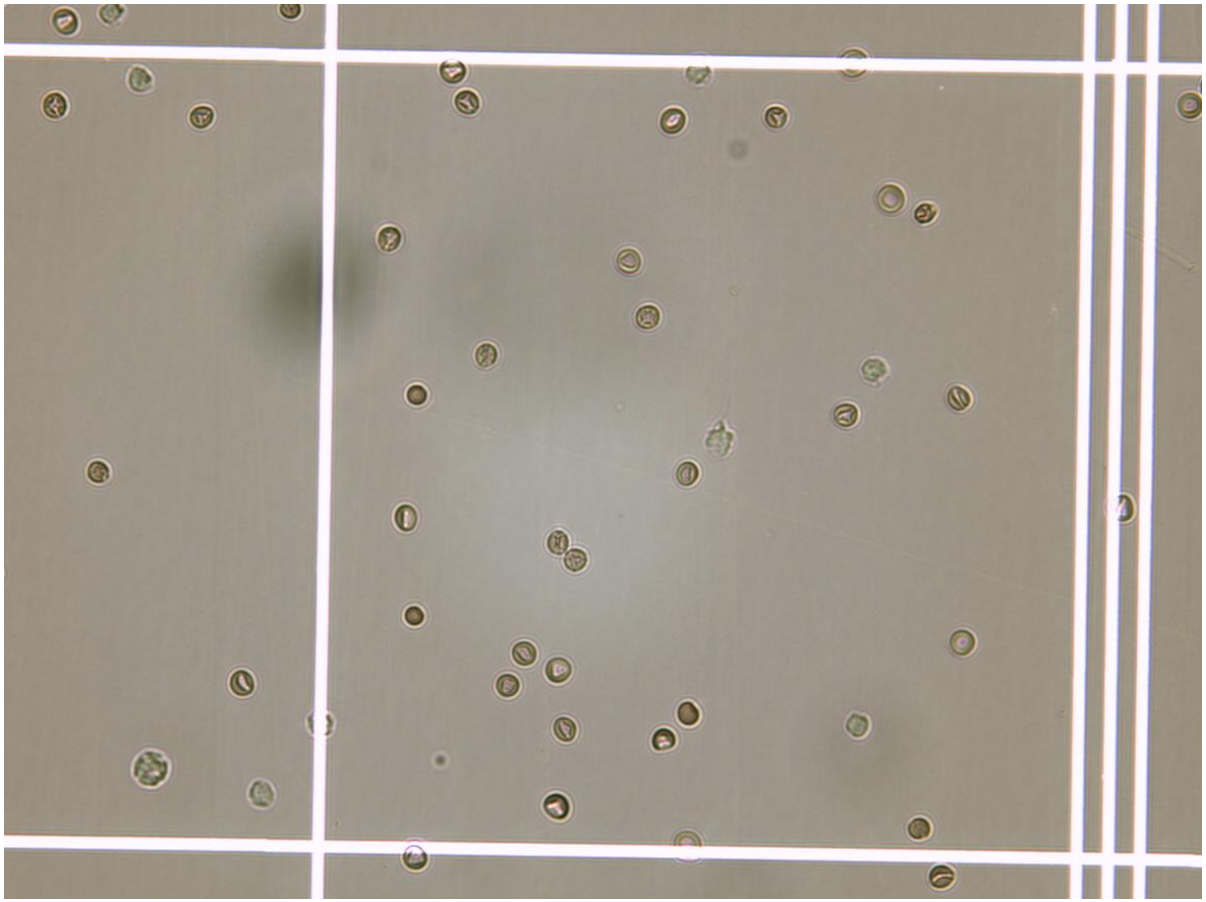
Leucocyte and erythrocyte count



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Summary On-Site Training

- correctly performed lumbar punctures
- accurate estimation of visual blood contamination
- correct leucocyte and erythrocyte cell counts

will ensure high quality of the CSF samples

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SIV follow-up

- Details of the visit will be summarised in a SIV Report and the site will be informed of the decision regarding inclusion within 20 days
- Sites will only be permitted to enrol participants after a favourable outcome is documented and received
- Additional training visits may be conducted to address specific issues at a site, e.g:
  - failure to meet recruitment targets
  - protocol violations
  - low yield or poor quality CSF
  - serum or plasma samples
  - inadequacies in data entry or record-keeping identified by routine monitoring procedures

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Monitoring

- Participation in HDClarity will not increase the frequency of remote or on-site data review for Enroll-HD unless:
  - Sites recruit a significant number of participants into Enroll-HD because of participation in HDClarity
  - New site staff are trained to carry out Enroll-HD core assessments
- If Enroll-HD core assessments are out of window and repeated at the HDClarity screening visit they are monitored by HDClarity CC

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Interim Monitoring Visits

- The IMV will be performed according to the Enroll-HD Monitoring Plan with the following additions:
  - Review HDClarity ERB/ REB/ IRB approval of revisions to ICF, if applicable
  - Review of any new HDClarity informed consent forms and ensure that the correct ICF version has been used and that the consent process is properly documented (correct signatures on the forms, etc.)
  - Verify eligibility of enrolled HDClarity participants per protocol criteria
  - Review of new and ongoing Reportable Events and SAEs and verifying adequate reporting and follow-up
  - Continued adequacy of study staff and facilities for HDClarity
  - Status of deficiencies noted during the previous HDClarity monitoring visit
  - Adherence to the HDClarity protocol, noting protocol violations
  - Perform Source Data Verification (SDV) for HDClarity

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