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AMBITION-*cm*
AMBIsome Therapy Induction OptimizatioN

Work Practice Document: 12
Lumbar Puncture

Title of study	High Dose AMBISOME© on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Phase III Randomized Controlled Non-inferiority Trial		
Acronym	Ambition-cm – AMBIsome Therapy Induction OptimizatioN		
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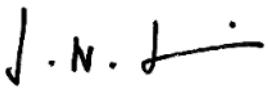
Approved by	Joseph Jarvis CI		20/07/2017

Revision History:		
Version Number	**Effective Date**	**Reason for Change**
1.0		First version

Working Practice Document 12: Lumbar Puncture

Purpose

This document describes how lumbar puncture will be performed by study staff.

References

1. Ellenby MS et al, "Performing Medical Procedures: Lumbar Puncture", NEJM 2006.
2. Adapted from Jesse Nussbaum, Standard Operating Procedure for Lumbar Puncture, Malawi
3. AMBITION Trial Protocol
4. Oxford Handbook of Clinical Medicine, 8th Edition, Oxford University Press, April 2010

Scope

This WPD applies to the process of managing patients with recurrent symptoms and possible IRIS

Materials

WPD 10: Management of raised intracranial pressure

Materials:

1. Sterile towel pack containing:
    a. 1 x plain towel
    b. 5 x gauze wrapped
    c. 1 x kidney bowl
    d. 1 x small specimen bowl
    e. 1 x fenestrated towel
2. Chlorhexidine (or iodine if not available)
3. 1 x 5- or 10-ml syringe/needle set
4. 2 x 20-gauge x 9cm spinal needles (yellow hub) or 22-gauge (black hub)
5. 1 x manometer
6. 1 x pair non-sterile gloves
7. 1 x pair sterile gloves

8. 3 x 5ml specimen tubes
9. 1 x 20ml or 30ml syringe
10. Local anaesthetic (1% or 2% lidocaine or 1% lignocaine)
11. Sharps bin – MUST BE AT BEDSIDE FOR IMMEDIATE SHARPS DISPOSAL

Procedure:

A. Explain the procedure

1. Outline the steps below for the patient or family member
2. List the relevant indications:
    a. Diagnosis of meningitis
    b. Release of intracranial pressure
    c. Follow progress of treatment
3. List the potential risks:
    a. Introduction of a new infection
    b. Cerebral herniation
    c. Subdural or subcutaneous haematoma
    d. Pain

B. Confirmation

1. Check that you have the correct patient
2. Make sure that there are none of the following contraindications:
    a. Platelets <20,000x10^6/L, patient on warfarin, on treatment dose heparin
    b. Cardiorespiratory compromise that prevents lateral positioning
3. Check that all the materials are present

C. Non-sterile preparation

1. Place patient in lateral recumbent position for manometer measurements

    a. Knees should be as close as possible to the chest, head down, and back flexed

    b. The spinal column should be parallel to the bed and the floor

2. Palpate the landmarks

    A line between the iliac crests intersects the L4 spinous process and the target intervertebral spaces, L3 and L4, are above and below respectively

3. Wearing non-sterile gloves, open the sterile towel pack

4. Taking care not to touch all the towels, take the top towel and place it on the bed in front of you, tucking it under the patient – this will collect excess blood or CSF that drips onto the bed

5. Open the syringe, spinal needle and manometer packaging onto the open sterile towels without touching them

D. Sterile preparation

PERFORM SITTING DOWN – this ensures comfort and facilitates accurate pressure reading

1. Don sterile gloves
2. Use the remaining gauze to coat the skin three times with chlorhexidine or a similar sterilant in widening concentric circles
3. Drape the skin with towels
4. The target intervertebral space should be visible through the fenestrated towel

E. Local anaesthesia

1. Draw up 1-2ml of local anaesthetic

2. Palpate the landmarks again to confirm the location of the intervertebral space

3. Inject subcutaneously, then deeper, into the intervertebral space

    a. Always withdraw on the syringe plunger as you advance the needle

F. Needle insertion

1. Palpate the landmarks again to confirm the location of the intervertebral space

2. Insert the spinal needle with stylet in place

    a. Insertion should be at the same site as the anaesthetic

    b. Insert at the superior aspect of the inferior spinous process

    c. Needle should be parallel to the floor, pointed toward the umbilicus

    d. Bevel should be pointed toward the ceiling

3. There may be a 'give' when the needle passes through the ligamentum flavum

4. The stylet should be removed at intervals to check for CSF flow

5. In no fluid is detected or bone is encountered, reposition the tip of the needle and try advancing again

    a. If unsure of the target direction, palpate again. Usually the tip of the needle will need to be angled more toward the head

    b. The needle may be withdrawn to the level of subcutaneous tissue

    c. Try not to exit the skin unless necessary

6. There may be blood encountered

    a. If there is a steady flow of venous blood, or if the needle is clogged with clotted blood, withdraw the needle and hold pressure

    b. The procedure may be attempted again at another intervertebral space using a fresh needle

G. Opening Pressure

1. When good flow is achieved, remove the stylet and immediately attach the manometer

2. Wait for the fluid to rise and stop, then record the reading

H. Collection

1. Keeping the manometer attached, turn the tap 90 degrees down to drain the CSF from the manometer.

2. Allow the CSF to drip into the three collection tubes

a. Never aspirate CSF – this may induce cerebral herniation

b. One tube may be used for culture, one for cell count, another for storage

c. If at a site participating in PK/PD, cryptococcal PCR, semi-quantitative CrAg titer or metabolic staining sub-studies please refer to the relevant WPDs as additional samples will be required

3. If the opening pressure is raised please refer to WPD 10: Management of raised intracranial pressure

I. Closing pressure

1. Turn the tap 90 degrees again to measure the closing pressure

2. If the opening pressure was >30cm the target closing pressure is <20cm

3. No more than 40ml of CSF should be removed

J. Completion and Cleaning

1. Replace the stylet and remove the needle

2. Hold pressure with a gauze or cotton until bleeding stops

3. Put a plaster or tape some gauze over the site

4. Record the total amount of CSF drained before discarding any

5. Place needles in the appropriate sharps box

6. Place other waste materials in the appropriate rubbish containers

7. Label the tubes with the patient's study code, date, and day number

Timing of LPs:

- LPs are to be performed on study admission (as part of routine patient care) and study days 7 and 14.

- A repeat LP may be required on admission if the diagnostic CSF sample is old/unavailable and/or the patient's CSF OP has not been measured.

- To calculate the early fungicidal activity (EFA) of a given regimen, 3 quantitative culture calculations, from 3 sequential LPs (on study days 0/1, 7 and 14), will be required for study purposes.

- If study day 7, for example, falls on a weekend, the study LP may be performed on the closest possible week day. If raised intracranial pressure is a clinical issue therapeutic LPs will be required over the weekend, regardless, and the CSF samples thus obtained will be used to perform study quantitative cultures.

Training

Each staff member receives or has direct access to applicable Working Practice Documents (WPDs).

Each staff member reviews the applicable WPDs once a year.

All WPD training is documented and tracked in the training log located in the Investigator Site File (ISF)

New staff are trained on applicable WPDs within 30 days of employment and all WPDs within 90 days of employment.

Staff members whose duties fall within this WPD scope are retrained within 14 days of the approval of each WPD revision.

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Staff signatures: (signing below indicate that you have read this WPD and understand the material contained in it)

Date	Name (Please print)	Signature