Supplemental Digital Content - Figure S1: CNS Infection flow sheet (Comprehensive)

**Name**
Suspicion for central nervous system infection (fever, headache, altered mental status, meningeal signs, etc)

**Date**

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### Lumbar Puncture (record opening pressure)

- □ CSF White Blood Cell Count (PMN, Lymphocyte)
- □ CSF glucose
- □ CSF protein
- □ Gram stain
- □ Bacterial culture
- □ AFB Ziehl-Neelsen stain (at least 6 mL)

Initiate Ceftriaxone 2g IV if symptom < 10 days. □ started □ no

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**Definite Bacterial Meningitis:**
- positive gram stain or culture in CSF
- or
- CSF PMN >50% + positive blood culture +
- CSF:serum glucose <0.5

**Possible BM:**
- CSF PMN >50% + CSF:serum glucose <0.5 + improvement on antibiotic treatment
  ➔ Bacterial Meningitis treatment

**Probable BM:**
- CSF PMN >50% + CSF:serum glucose <0.5 + one of the following:
  - Active TB on CXR
  - AFB found in sample other than from CSF
  - Clinical evidence of other extrapulmonary TB
  ➔ Bacterial Meningitis treatment

**Definite Tuberculous Meningitis:**
- Acid fast bacilli in the CSF
  ➔ Treat tuberculous meningitis

**Cryptococcal meningitis:**
- Positive India ink or serum/CSF cryptococcal antigen

**Possible Viral Meningitis:**
- CSF finding (lymphocytes >50% and CSF:serum glucose >0.5)

**Other abnormal CSF findings in Non-HIV patients:**
- Continue BM treatment
- Consider IRIS if lymphocytic predominance and on ART

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**Repeat Lumbar Puncture**
- □ AFB stain (at least 6 mL)
- □ leukocyte count with diff □ CSF protein & glucose
- □ Gram stain □ CSF bacterial culture
  ➔ Consider TBM therapy if rise in CSF/serum glucose <100%

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Definite diagnosis or improvement within 48 hours?

**Yes**
- Continue Treatment

**No**

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Figure S2: CNS Infection flow sheet (Stepwise)

Suspicinon for central nervous system infection (fever, headache, altered mental status, meningeal signs, etc)

NOTES:
- If CRAG is not available, use India Ink
- Additional rule-out: Malaria smear, VDRL, Toxoplasmosis IgG before viral determination (cost not included in above estimate)

<table>
<thead>
<tr>
<th>CRAG</th>
<th>CRAG Positive</th>
<th>CRAG Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRAG Positive</td>
<td>Treat TBM</td>
<td>Stop, Consider Other Diagnostics</td>
</tr>
<tr>
<td>CRAG Negative</td>
<td>CSF glucose</td>
<td>CSF Protein</td>
</tr>
<tr>
<td>Normal &gt;50% serum</td>
<td>Low &lt;50% serum</td>
<td>Normal &lt;50 mg/dL</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
<td>Low &lt;50%</td>
<td>High &gt;50</td>
</tr>
<tr>
<td>Normal &lt;50 mg/dL</td>
<td>High (&gt;50)</td>
<td>Normal &gt;50%</td>
</tr>
<tr>
<td>Consider other Diagnoses</td>
<td>Viral, Provide Supportive Care</td>
<td></td>
</tr>
</tbody>
</table>

Treatment Regimens:
- **Bacterial meningitis WHO** recommended treatment:
  - Ceftriaxone 2g/day IV/IM x 5 days
- WHO Cryptococcal Guidelines at: [who.int/hiv/pub/cryptococcal_disease2011](https://who.int/hiv/pub/cryptococcal_disease2011)

Abbreviations:
CRAG = Cryptococcal Antigen
AFB = acid fast bacilli, Ziehl-Neelsen Stain
TBM = TB meningitis
*Xpert MTB/RIF Assay or other enhanced TB diagnostic*
Figure S3: CNS Infection flow sheet (Minimalist)

Suspicion for central nervous system infection (fever, headache, altered mental status, meningeal signs, etc)

CRAG LFA

CRAG LFA

Negative

Positive

WBC >5

Cryptococcal Treatment

Refer to WHO cryptococcal guidelines

NOTES:

• If Ceftriaxone treatment was initiated prior to obtaining LP, do not run CSF Bacterial Culture, but instead check CSF glucose.

• Additional rule-out: Malaria smear, VDRL, Toxoplasmosis IgG before viral determination (cost not included in above estimate)

• Bacterial meningitis WHO recommended treatment:
  Ceftriaxone 2g/day IV/IM x 5 days

Abbreviations:

CRAG = Cryptococcal Antigen
AFB = acid fast bacilli, Ziehl-Neelsen Stain
LFA = lateral flow assay

Stop
Pursue other Diagnostics

PMN > 50%

Bacterial Meningitis Treatment

Gram Stain

Positive

Negative

Bacterial Meningitis Treatment

AFB Stain

Positive

Negative

CSF Bacterial Culture (if Antibiotics not administered)

Abnormal

Negative / Normal

Bacterial Meningitis Treatment

Continue Therapy

Possible Viral Meningitis
Provide Supportive Care

Reassess in 48 hours.
If no response, recheck CSF glucose

CSF Glucose Normalized

CSF Glucose Abnormal

Consider TBM Treatment