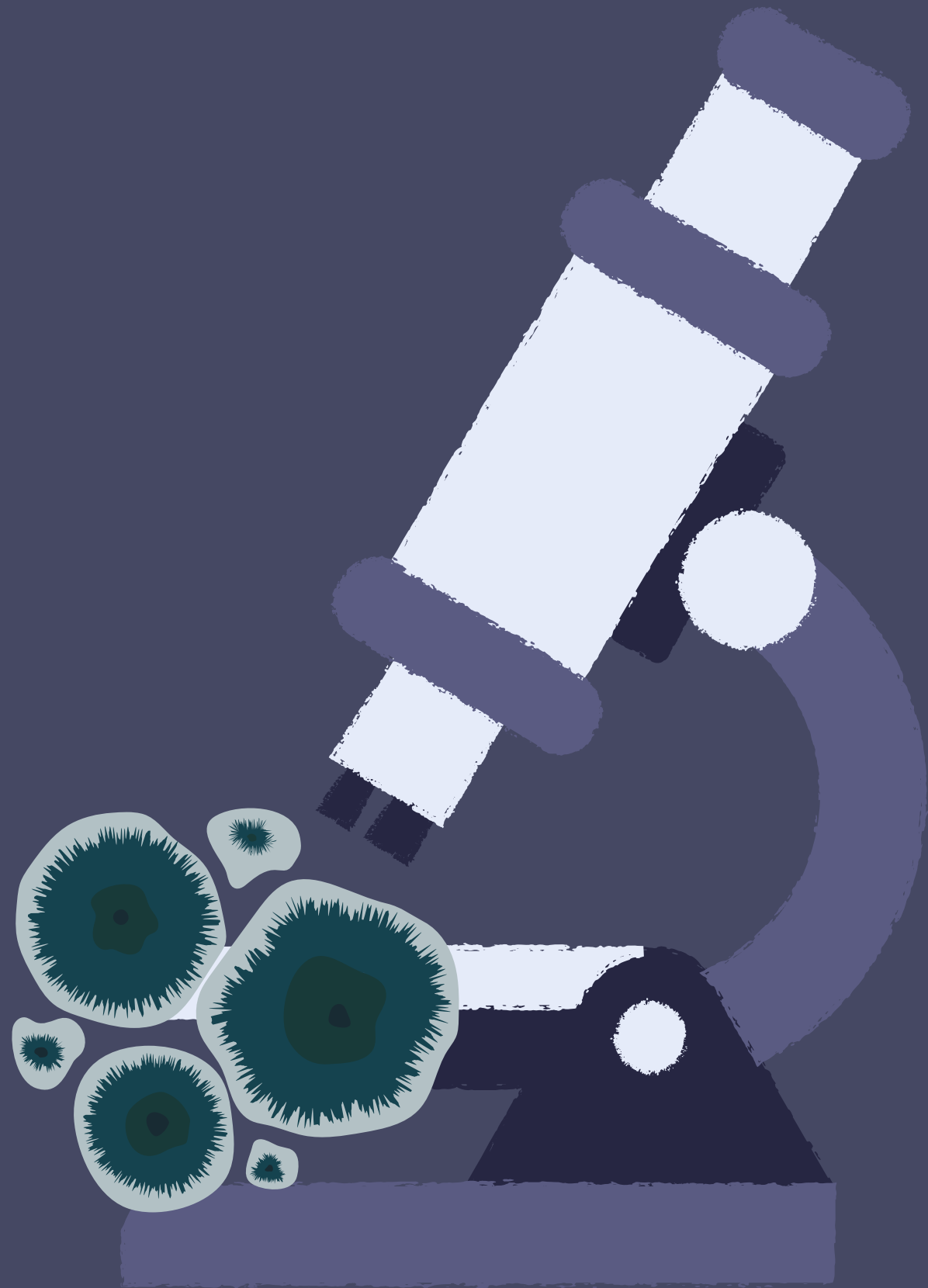


CASE STUDY 7

VORICONAZOLE IN CRYPTOCOCCAL MENINGITIS

WONG E-JINQ
AMS PHARMACIST





CRYPTOCOCCAL MENINGITIS

- Cryptococcus infections in the brain common found in immunocompromised patients.
- Recommended treatment:
 - Amphotericin B
 - Fluconazole
 - +/- Flucytosine

SAPM

Male

39y

Medical history:

Hypertension

Retroviral disease (treatment naive)

BP: 136/75mmHg

PR: 64bpm

SpO2: 100% under RA

Referred from district hospital

Presented with:

Headache x2weeks

- Frontal area with prickling in nature

Feverish x 2weeks

Vomiting x 7days

- 3-4 times per day with food & fluid content

CECT:

? lesion over Left
temporoparietal region

Impression:

Persistent headache for investigation TRO Space-
occupying Lesion

Plan:

Start IV Ceftriaxone 2g BD

IV Acyclovir 500mg TDS

KIV for Bactrim

RVD

CD4: 42

Treatment naive

Persistent headache

WHAT ARE THE POSSIBLE DIAGNOSIS?

A Toxoplasmosis

B Cryptococcus
meningitis

C Tuberculous
Meningitis



RVD
CD4: 42
Treatment naive
Persistent headache

CYPTOCOCCAL MENINGITIS

INVESTIGATIONS:

- Lumbar puncture done.
- CSF
 - Culture & Sensitivity
 - Biochemical & Cell Count

CSF RESULT:

Cryptococcus Neoformans

Glucose: 2

Protein: 1642

WBC count: nil

Lymphocyte: nil



Amphotericin B

Fluconazole

+/- Flucytosine

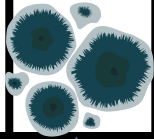
RECOMMENDED ANTIFUNGAL THERAPY

TREATMENT PROGRESS

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|
| IV Amphotericin B 45mg OD (0.7mg/kg) | | | | | | | | | | | | | | | | | | |
| Tab. Flucytocine 1.25g QID | | | | | | | | | | | | | | | | | | |
| Cap. Fluconazole 400mg TDS | | | | | | | | | | | | | | | | | | |

SrCr (mmol/L): 55 → 78 → 84 → 104 → 110 → 132

TREATMENT PROGRESS

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|----------------------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|
| |  | | | | | | | | | | | | | | | | | |
| IV Amphotericin B 45mg OD | | | | | | | | | | | | | | | | | | |
| Tab. Flucytocine 1.25g QID | | | | | | | | | | | | | | | | | | |
| Cap. Fluconazole 400mg TDS | | | | | | | | | | | | | | | | | | |

CSF:

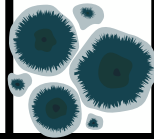
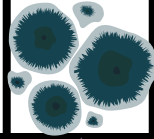
Culture & Sensitivity: ***Cryptococcus Neoformans***

Glucose: 1.8

Protein: 1643

Indian Ink: Encapsulated cell seen

TREATMENT PROGRESS

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|----------------------------|--|---|---|---|---|---|---|---|---|----|----|----|---|----|----|----|----|----|
| |  | | | | | | | | | | | |  | | | | | |
| IV Amphotericin B 45mg OD | | | | | | | | | | | | | | | | | | |
| Tab. Flucytocine 1.25g QID | | | | | | | | | | | | | | | | | | |
| Cap. Fluconazole 400mg TDS | | | | | | | | | | | | | | | | | | |

CSF:

Glucose: 1.8

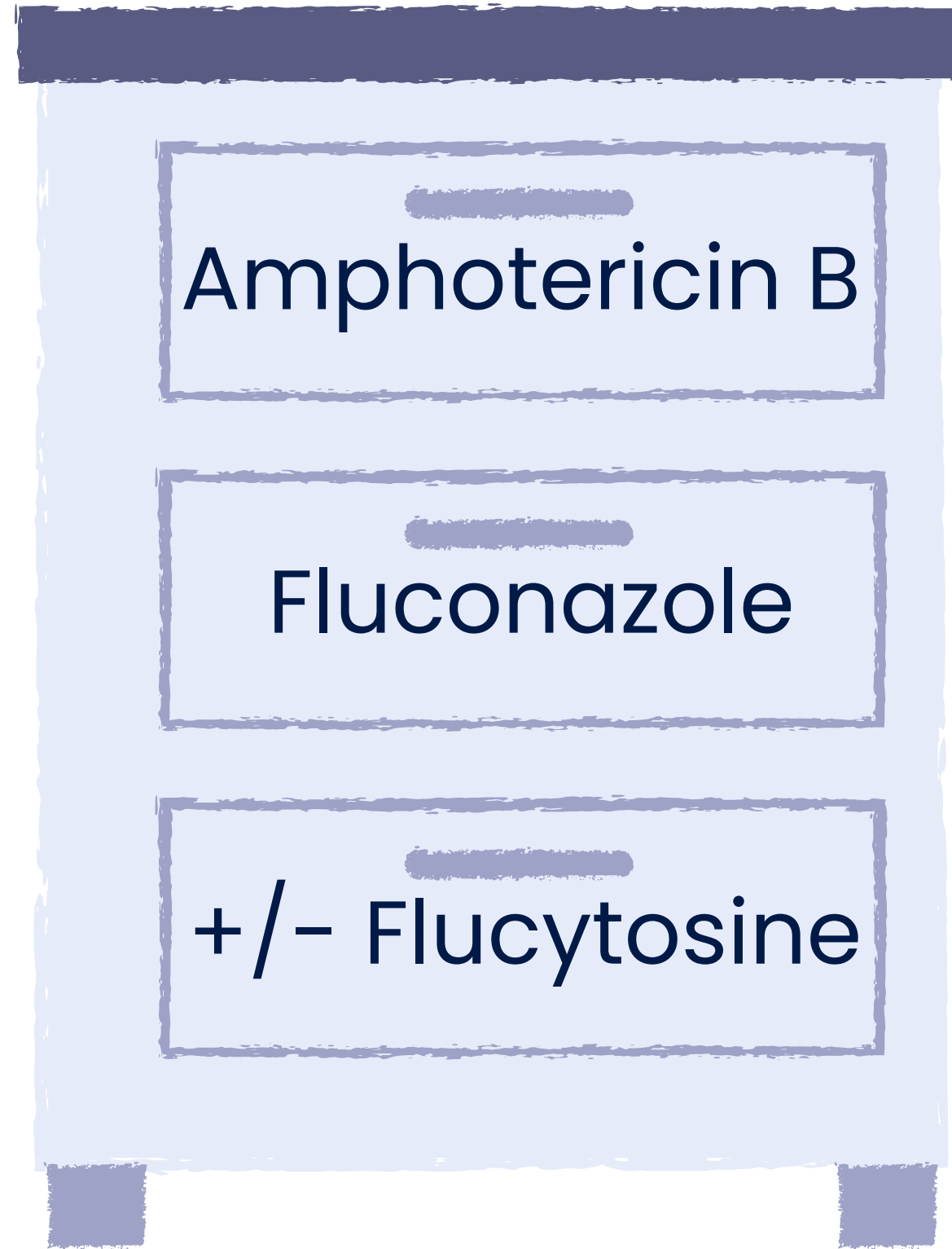
Protein: 1643

WBC: 81

Lymphocytes: 88%

Culture & Sensitivity: ***Cryptococcus
Neoformans***

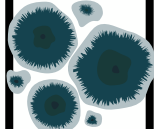
Indian Ink: Encapsulated cell seen



RECOMMENDED ANTIFUNGAL THERAPY

**WHAT TO DO WHEN THEY
DOESN'T WORK?**

TREATMENT PROGRESS

| | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 |
|----------------------------|----|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| | |  | | | | | | | | | | | | | | | | | |
| IV. Voriconazole 250mg BD | | | | | | | | | | | | | | | | | | | |
| Tab. Voriconazole 250mg BD | | | | | | | | | | | | | | | | | | | |

CSF:

Glucose: 2.0

Protein: 1031

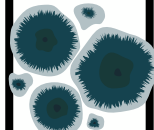

WBC: 29.7

Lymphocytes: 93%

Culture & Sensitivity: ***Cryptococcus
Neoformans***

TDM Voriconazole: (8/12/2024).
1.08ug/ml

TREATMENT PROGRESS

| | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 |
|----------------------------|----|---|----|----|----|----|----|----|---|----|----|----|----|----|----|----|----|----|----|
| | |  | | | | | | |  | | | | | | | | | | |
| IV. Voriconazole 250mg BD | | | | | | | | | | | | | | | | | | | |
| Tab. Voriconazole 250mg BD | | | | | | | | | | | | | | | | | | | |

CSF:

Glucose: 1.8

Protein: 829

WBC: 48.3

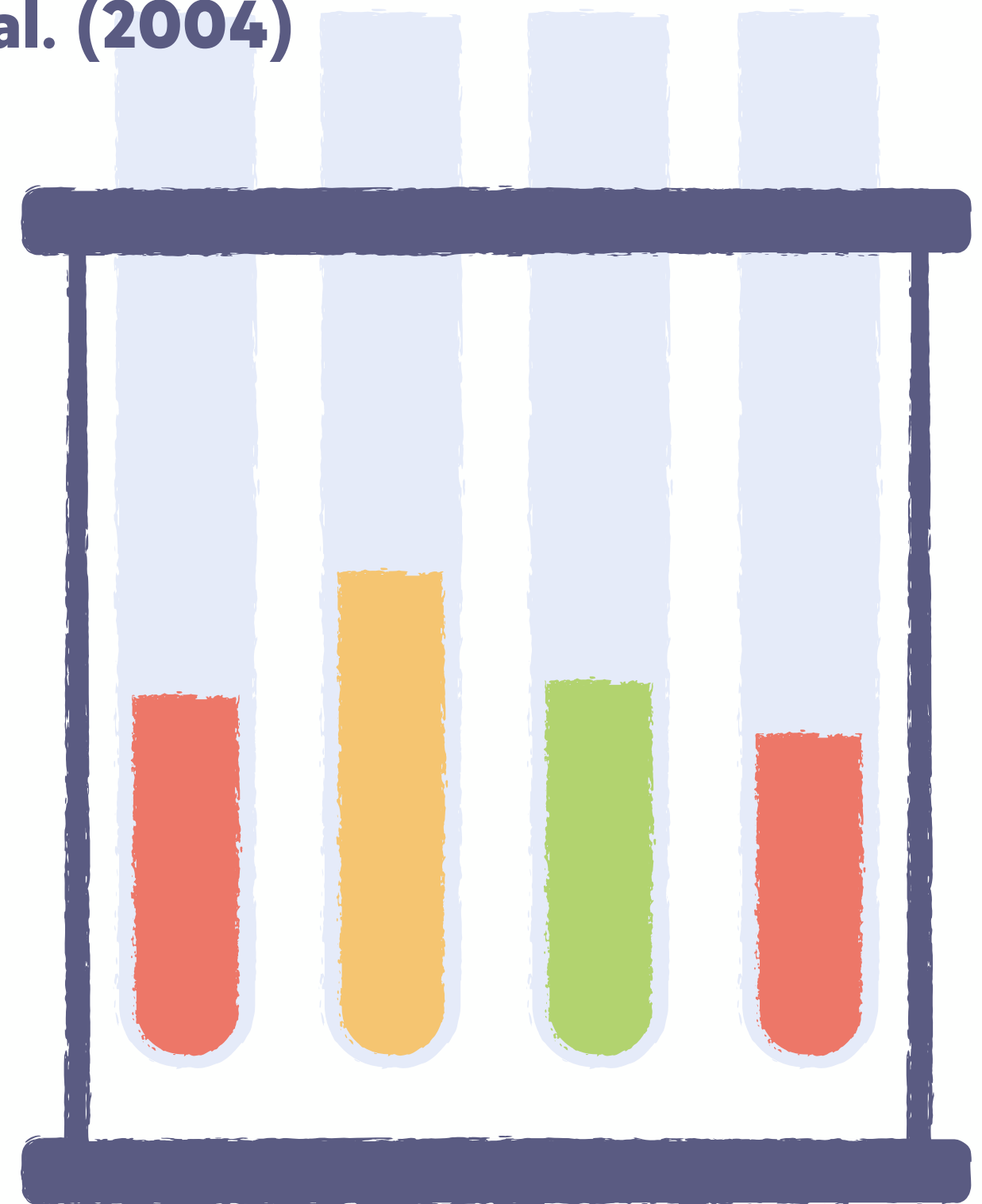
Lymphocytes: 88%

Culture & Sensitivity: **No Growth**

Why Voriconazole on Cryptococcus Neoformans?

van Duin DCleare W et al. (2004)

- Voriconazole shows lowest MIC among others antifungals (Ampho B, Itraconazole & Fluconazole)
- Voriconazole penetrates into the cerebrospinal fluid
- Fungicidal to C. neoformans
- Additional advantage:
 - Reduce cellular capsular volume
 - Antifungal activity NOT affect by the melanization of C. neoformans



Is Voriconazole an alternative?

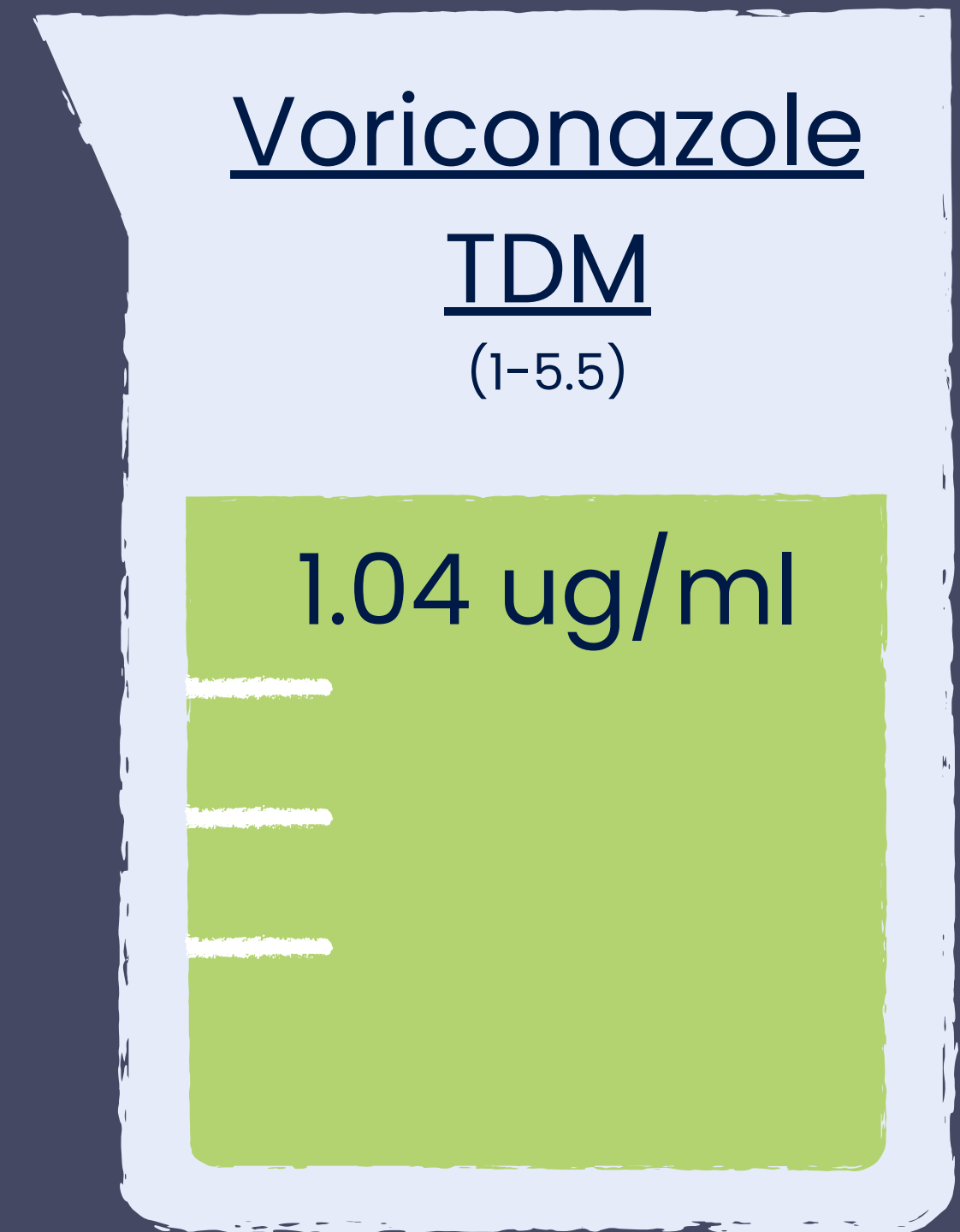
Case studies and Clinical trials support use of Voriconazole in treating CM.

Yao, Y. et al. (2015) N=55 patients

- Recommend Voriconazole for CM, especially to patients who had a treatment failure with amphotericin B alone or accompanied by fluconazole.

Ngan, N.T.T. et al. (2022)

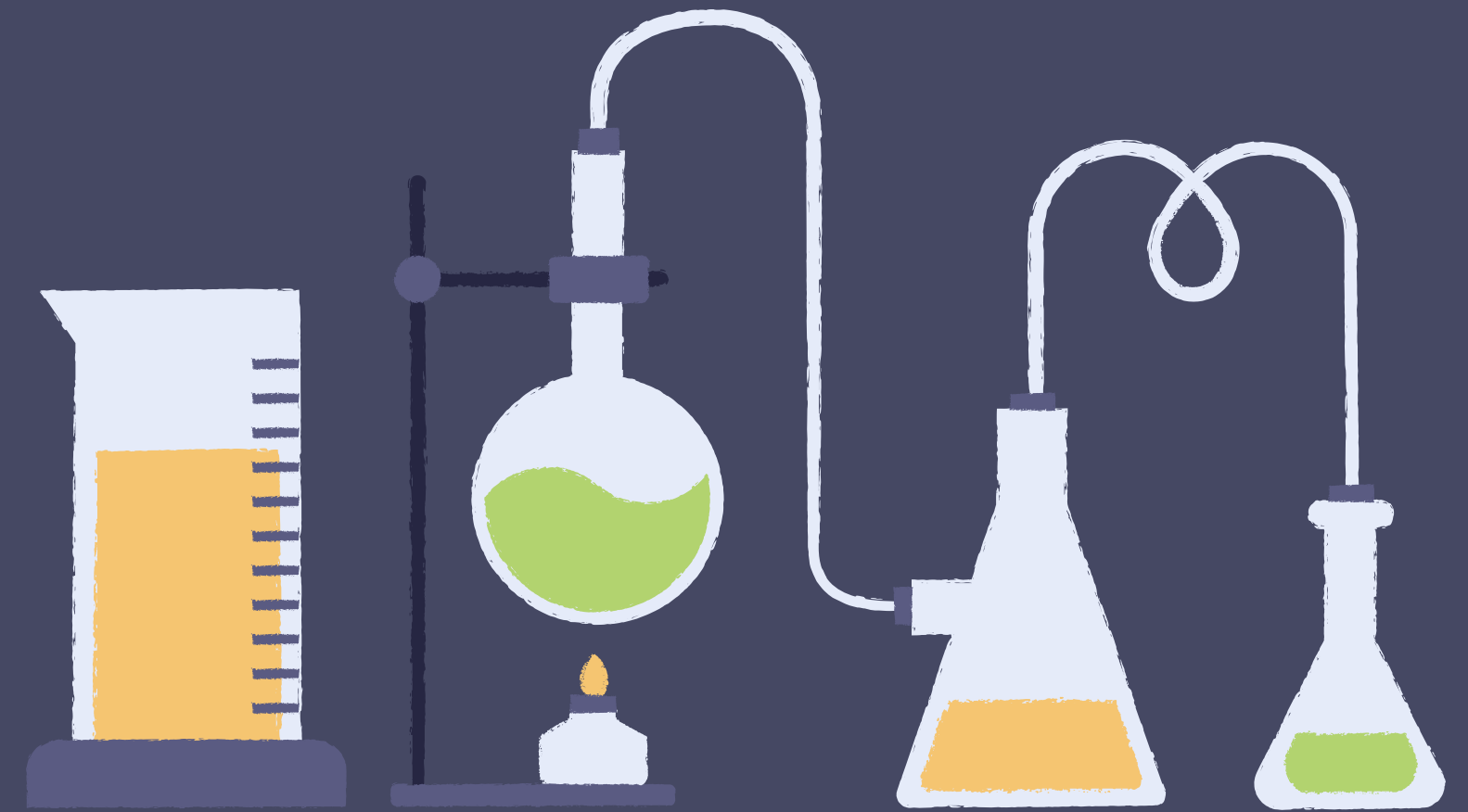
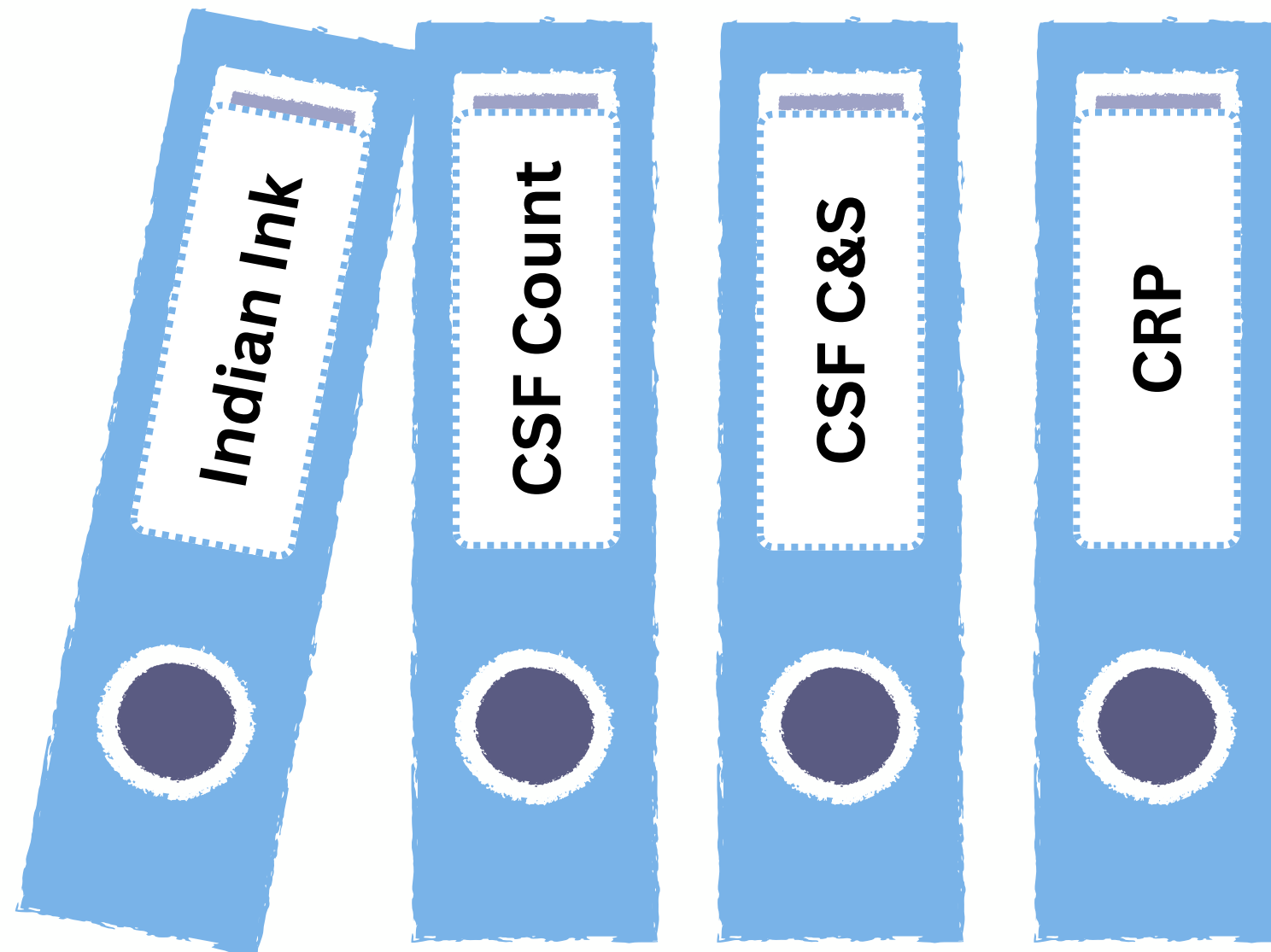
- Voriconazole, in combination with flucytosine, is currently being evaluated as an option for induction therapy for cryptococcal meningitis



WHAT DOES THIS MEAN?

Which is significant?

How do we interpret them?



- Culture & Sensitivity VS Indian Ink
- CSF Count & CRP
- Relate clinical response



SUMMARY

More clinical trials or clinical evidences with bigger sample size requires to support and the use of Voriconazole in Cryptococcus Meningitis infection.

- Voriconazole TDM level plays an important role in this case, especially in cases with less clinical practice or off-label use.
- In particular where dosing optimization is crucial where patient do not response to recommended treatment.



THANK YOU!

ANY QUESTIONS?

