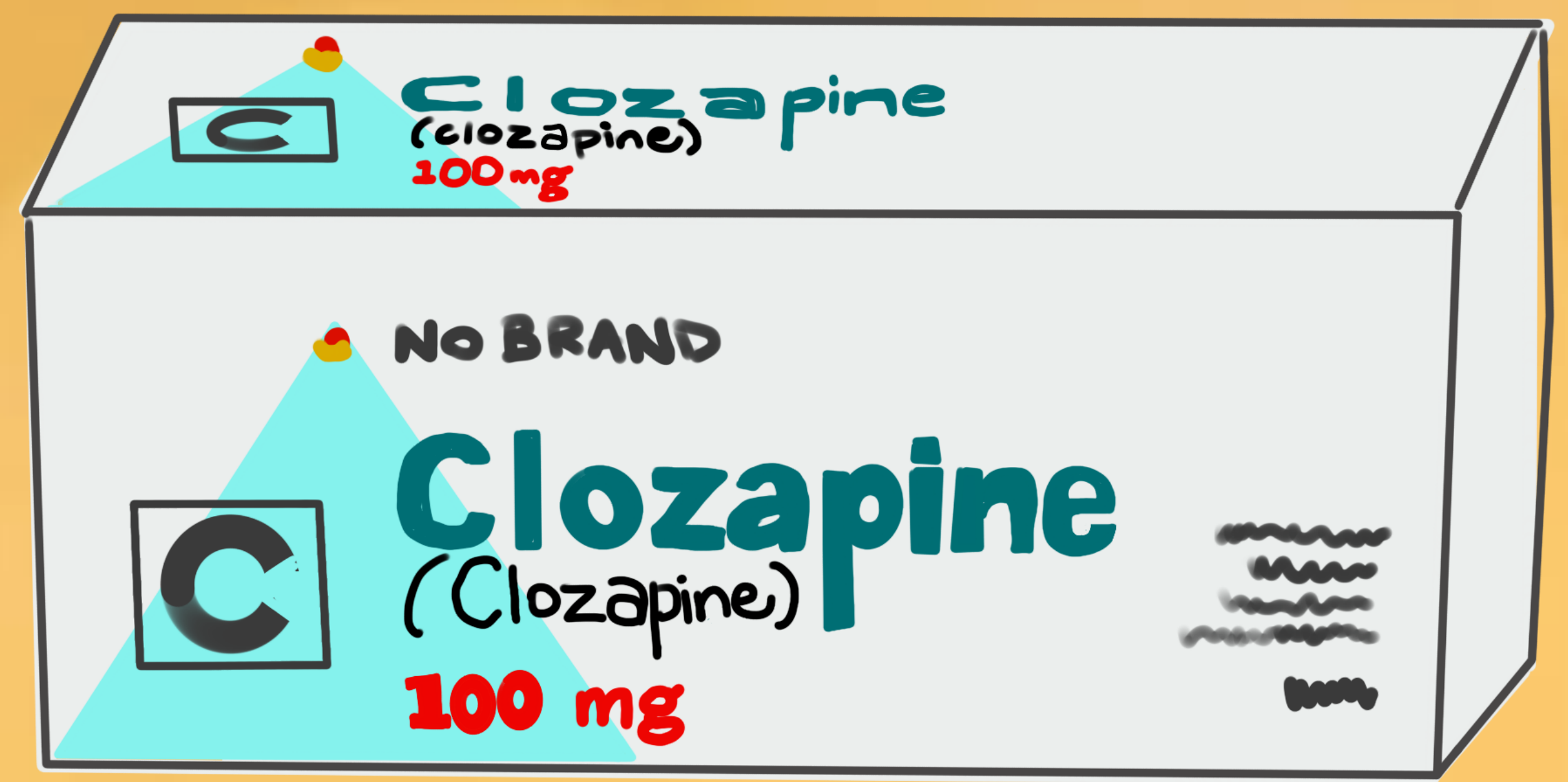


# Riding the Wave of Clozapine Levels and Respiratory Illness



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## Clinical Features

- 67 year old male admitted with a fever
- Symptoms of tachycardia and delirium
- History of Schizophrenia; Medications included - Clozapine 350mg nocte Sodium Valproate 200mg mane 700mg nocte
- Has been a smoker of 15-20 cigarettes a day

GeneXpert Influenza PCR

Specimen: Swab Nasopharyngeal

Influenza A **DETECTED**  
 Influenza B **Not Detected**  
 Respiratory Syncytial Virus **Not Detected**

Time/Date	Spec	HGB	WBC	PLT	NEUT
c 09:36 18-Jun-19	BL000	119 L	10.5	693 H	6.89
c 09:17 17-Jun-19	BL000	116 L	8.5	558 H	5.86
c 11:45 13-Jun-19	BL000	114 D	6.3	195	4.46
c 16:40 11-Jun-19	BL000	127 L	8.4	160	6.87


3 days prior to admission

Normal WCC and Neutrophils  
 CRP =25

## Literature Review <sup>1</sup>

- **77%** Schizophrenia cases encounter elevated clozapine levels due to infection
- **57.5%** of infections are **respiratory**
- **20%** of patients have **delirium**

## Patient Journey

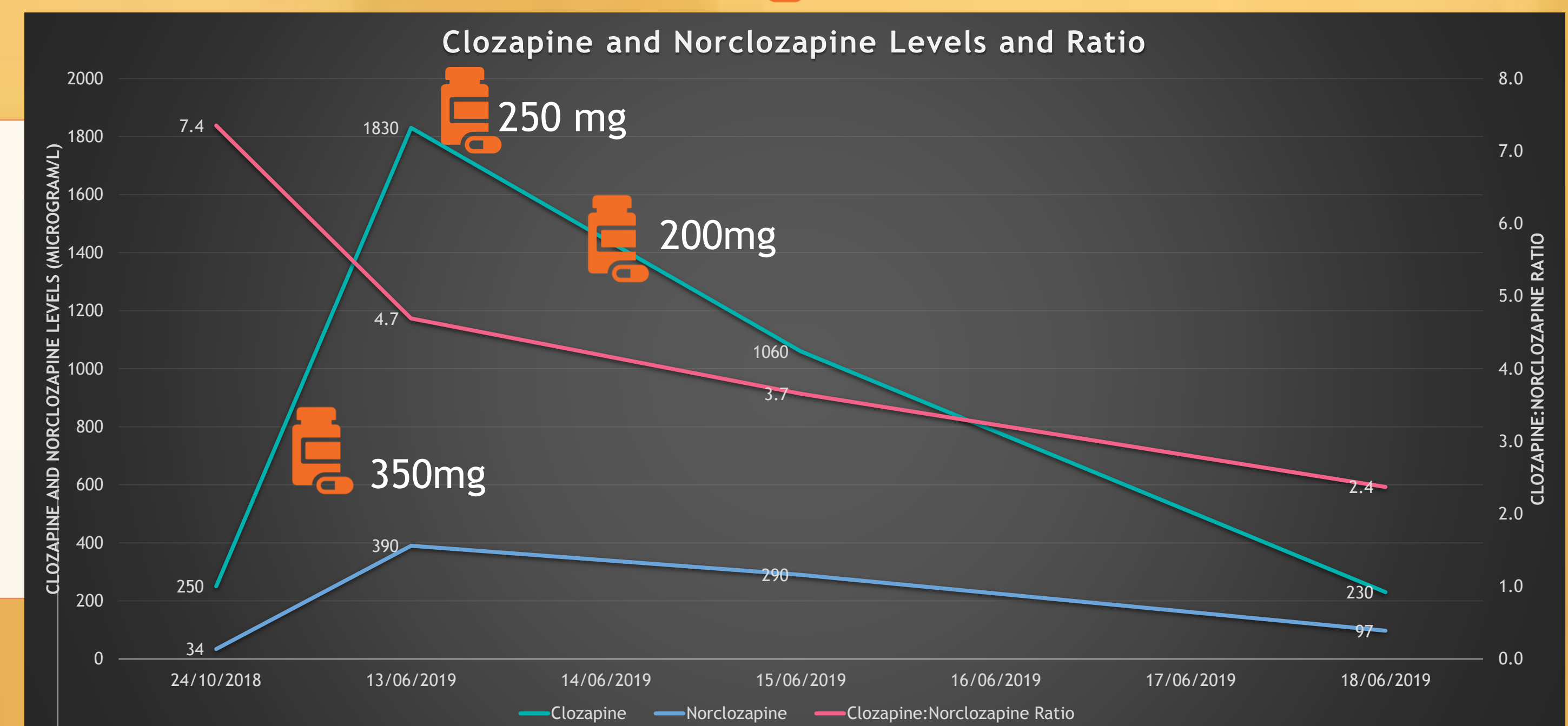
- Tamiflu for 5 days
- Hypersalivation on Day 2 treated with atropine eye drops
- Delirium resolved
- Nil seizures  On sodium valproate as a mood stabiliser

## Discussion

- Increased **inflammatory mediators** such as IL-6-TN- $\alpha$  interferon & CRP reduces CYP1A2 expression by up to 90% causing reduced clozapine metabolism and increased Clozapine:Norclozapine ratio. Acute infection can also change other metabolic pathways.<sup>1,2</sup>
- Clozapine is **95% bound in plasma** to alpha-1 glycoprotein (AGP), which is known to increase several fold in infection - **↑ binding and inactivation of clozapine**. Hence levels may not always correlate with symptom severity
- ↑ seizure risk at clozapine levels >600mcg/L.<sup>1,3</sup>

## Learning Points

- Understand effects of infection and smoking cessation on clozapine.
- To be aware of specific dose related side effects and management
- Understand the effect of concurrent drugs on clozapine levels and side effects
- Recommend prompt monitoring of **clozapine levels** for patients admitted with **infection or change in smoking status**.
- Advocate for **early involvement** of Mental Health team for assessment and gradual dose titrations



70% of clozapine is metabolised to norclozapine via CYP1A2 - **infections downregulates CYP1A2**

Respiratory infections in smokers can lead to reduced smoking or reduced absorption of polyaromatic hydrocarbons so that enzyme induction is lost = **↑ Clozapine**<sup>3</sup>

### Dose-related Clozapine Side Effects

- Delirium
- Sedation
- Seizures
- Arrhythmias
- Hypotension
- Hypersalivation

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### References:

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2. Darling, P; Hutwaite, M. Infection -Associated Clozapine toxicity. Case Report. Clinical Schizophrenia and Related Psychosis 2011.
3. Interpretation of Clozapine levels. Graylands Hospital Drug Bulletin. North Metropolitan Health Service-Mental Health. April 2017. Vol 24 NO1. ISSN 1323-1251