### An Option for Clozapine Monitoring

**Fellow Name:** Samantha Kamp, MD  
**Faculty Mentor:** Laurence Guttmacher, MD

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**Introduction:**

Schizophrenia affects around 1% of the people in the world at some point in their lifetime. Clozapine remains the most effective antipsychotic available today for individuals with schizophrenia who do not respond to first line antipsychotic treatment — it should be third line drug used — or have persistent suicidal ideation or aggressive behavior. However, monitoring remains a significant barrier to prescription and treatment adherence. Data indicates, however, that most patients receive clozapine years after they would be good candidates for it, and many may never receive clozapine at all. Improved access to clozapine could benefit millions of patients and could result in substantial cost savings to the entire health care system. To assist in increasing the usability of clozapine and improve compliance, there are alternative monitoring options available.

### REMS Clozapine Treatment Recommendations and ANC Monitoring Guidelines:

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>Treatment Recommendation</th>
<th>Frequency of ANC Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>No treatment changes</td>
<td>Weekly</td>
</tr>
<tr>
<td>Elevated</td>
<td>Increased monitoring</td>
<td>Daily</td>
</tr>
<tr>
<td>Severe</td>
<td>Immediate discontinuation</td>
<td>As needed</td>
</tr>
</tbody>
</table>

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**Abstract:**

Despite having been in use for over 60 years, Clozapine is often overlooked as a potential source of severe side effects and due to the need for constant and continuous monitoring. Alternative monitoring options may be a way to increase provider and patient comfort around the usage of Clozapine.

**Discussion:**

Several anonymous surveys were given to prescribers to identify and rank the importance of barriers to Clozapine use and identify potential solutions [4, 5]. The need for close monitoring, regular blood work, and potential for non-adherence to blood work, the highest concern overall, were reported as the greatest clinical barriers. Solutions surveys found that point of care fingerstick [4] and among nine solutions, the ability to obtain lab results in the physician's office or pharmacy was top ranked. [5]

Severe neutropenia (ANC <500/µL) due to clozapine is well documented, leading to serious infections and even death in about 0.8% (or less) of treated patients. The required weekly ANC monitoring for 6 months places a large burden on patients, caregivers, and clinical staff, contributing to lower drug utilization rates and patient non-adherence. There are several Point-of-care (POCT) devices that are FDA approved to measure total white blood cell counts and differential counts in capillary or venous whole blood using a finger pricker method. Portable mass spectrometry devices, lab-on-a-chip (LOC) and smartphone applications (apps), can return results in less than 15 min from a single drop of blood. [10] White blood cell count correlation between the POCT device and routine laboratory methods in measuring WBC and neutrophil counts in venous samples being 0.95-0.99. [7, 8]

Correlation between capillary samples using the device and routine methods (venous sample) was 0.77 and 0.82 for WBCs and neutrophils, respectively. [7] Another study by Schalk et al[12] which studied 447 blood samples found no difference in the ANC between the two sample sets.

A study to determine whether fingerprick blood and plasma clozapine levels were equivalent to arm venipuncture blood and plasma levels for the purpose of therapeutic monitoring found that a fingerprick blood sample of 50 micro L was sufficient to measure clozapine levels accurately at steady state. [6]

A randomized cross-over trial have shown that consistent favoring of capillary blood testing as a significant or venous whole blood using a finger prick method. Portable mass spectrometry devices, lab-on-a-chip (LOC) and smartphone applications (apps), can return results in less than 15 min from a single drop of blood. [10] White blood cell count correlation between the POCT device and routine laboratory methods in measuring WBC and neutrophil counts in venous samples being 0.95-0.99. [7, 8]

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A randomized cross-over trial have shown that consistent favoring of capillary blood testing as a significant number of patients reported less pain and anxiety, greater convenience, less fear, and a better understanding of the intended purpose of sample collection. [8] There have been several FDA approved POCT devices which can return results within 5 minutes and some have the ability to deposit ANC results automatically into the REMS system.

My project has been creating a process to utilize finger-prick blood clozapine levels and to monitor ANC levels. This can be done in the hospital or outpatient setting as follows:

1. To obtain a capillary ANC and/or a CBC with diff:  
   - Get a microtainer with a purple/lavender capillary tube
   - Obtain blood sample
   - Create a text blood order in Epic
   - Send sample to 911 tube station

   **Note:** This is the procedure for in hospital testing at this time.

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**References:**