



Clinical Pharmacology & Toxicology Pearl of the Week

~ Drug-Induced Neutropenia ~

Drug-Induced Neutropenia (DIN) is a potentially serious consequence of many medications

It occurs via two pathophysiologic mechanisms:

1. Direct toxicity on granulocyte precursors in the bone marrow → decreased neutrophil production
2. Immune-mediated destruction:
 - Drug attaches to neutrophil → Antibody-mediated destruction (Fig.1)
 - Drug induces antibody formation → drug-antibody complex binds to the neutrophil, activating complement-mediated cell lysis (Fig. 2)
 - Drug + serum protein → drug-protein complex attaches to neutrophil membrane & stimulates antibody formation leading to complement-mediated cell destruction (Fig. 3)

Often these reactions are due to so-called “reactive” drug metabolites rather than the parent drug

Average time to onset varies by drug, ranging from 1 – 6 months

The most common drugs are antibiotics, antithyroid drugs & clozapine

Patients often present with signs of infection, fever and sore throat

Establishing a diagnosis includes:

- Presence of an Absolute Neutrophil Count (ANC) of $< 1.5 \times 10^9$ neut/L
- Absence of other causes (congenital vs. acquired)
- Patient is on a potential culprit drug

Management involves:

- Assess & manage ABCs in the setting of possible sepsis
- Evaluate for & treat Febrile Neutropenia as per local practice guidelines
- Stop the suspected drug; time to ANC recovery is 9 – 24 days
- The use of GCSF is controversial, Hematology should be involved for expert guidance
- Lifelong avoidance of the culprit drug is advised, and re-challenge is not recommended

The Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Specialist Link. Our service is also listed in the [Alberta Referral Directory](#). Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found [HERE](#).

More CPT Pearls of the Week can be found [HERE](#).

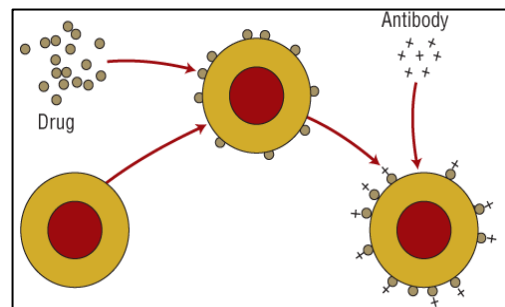


Figure 1: Drug Adsorption Mechanism

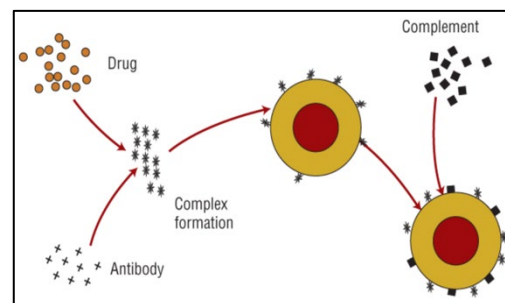


Figure 2: Innocent Bystander Mechanism

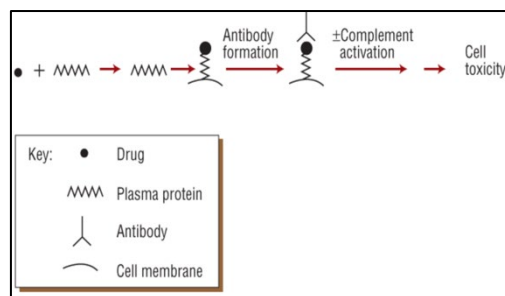


Figure 3: Protein Carrier Mechanism