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)

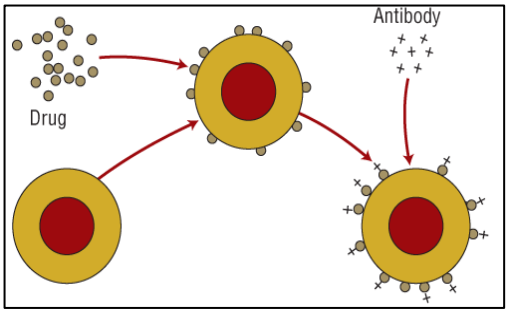

Figure 1: Drug Adsorption Mechanism

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

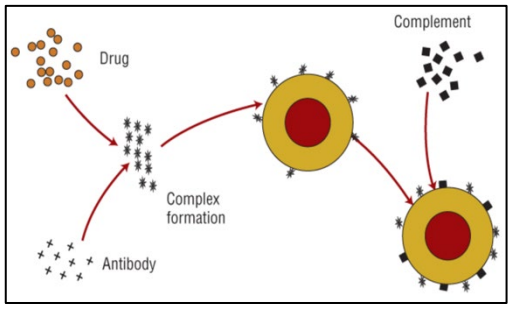

Figure 2: Innocent Bystander Mechanism

Establishing a diagnosis includes:

- Presence of an Absolute Neutrophil Count (ANC) of < 1.5 x 10^9 neuts/L
- Absence of other causes (congenital vs. acquired; explained HERE)
- Patient is on a potential culprit drug (click HERE for more details)

Management involves:

- Assess & manage ABCs in the setting of possible sepsis
- Evaluate for & treat Febrile Neutropenia as per local practice guidelines (Alberta Health Services Guideline for FN)
- 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

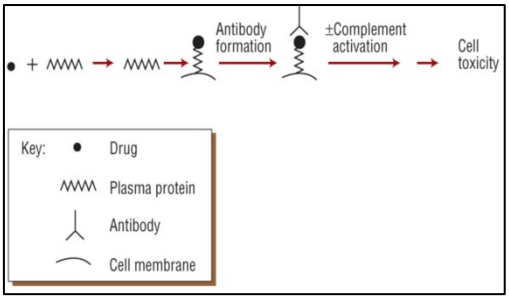

Figure 3: Protein Carrier Mechanism

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click HERE for clinical issues the CP service can assist with.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.