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Dear Colleague:

Re: Agranulocytosis in cocaine users.

Public Health in Edmonton and area has recently been made aware of and is monitoring cases of agranulocytosis that appear to be related to cocaine use. The agranulocytosis is not thought to be due to the drug but instead due to an adulterant or cutting agent, levamisole, a known cause of agranulocytosis in susceptible individuals. We are indebted to Dr. Don LeGatt, the laboratory clinical toxicologist who has provided evidence for the levamisole connection and to Drs. Robert Turner, Nancy Zhu, and Loree Larratt and their fellow hematology colleagues: and Dr. Francesco Mosiaco, his colleagues at the Boyle McCauley Health Center, who made us aware of these unusual presentations.

As of today 5 cases but 6 episodes (one patient presented twice) have been reported to us. Five presented to facilities in Edmonton and area and one in Grande Prairie. The first presentation was in July, one in August and four in November. The most recent three of these presented on November 16 and 17. The cases range in age from 18 to 48, and presented most often with febrile neutropenia. Many of these patients developed sepsis with one requiring intensive care admission.

The neutropenia is acute and profound, commonly with a neutrophil count of zero. The total white blood cell count may only be slightly below normal as the lymphocytes and other white blood cells are often normal.

In a cocaine user or suspected cocaine user, any symptoms of infection including fevers warrant an urgent CBC and differential to look for neutropenia. Urine toxicology should also be sent simultaneously looking for cocaine and levamisole. If the neutrophil count is less than 1 and the patient is febrile or has an active infection, **an urgent referral to an on-call Hematologist** should be made. The patient will require admission to hospital immediately, an infectious work-up including blood cultures should be undertaken and broad-spectrum intravenous antibiotics (ie. Piperacillin/Tazobactam, Imipenem or Ceftazidime) administered. Filgastrim (G-CSF) should not be started until consultation with a hematologist has been made. An additional investigation that can aid in the diagnosis is an elevated aPTT from a lupus anticoagulant which has been seen as well. Recovery generally occurs after 7-10 days, but close monitoring is required as the risk of mortality from sepsis is high.

A spot urine specimen (minimum 10 mL) should be collected for cocaine metabolite and levamisole toxicology testing **as soon as possible** – the latter drug has a short detection “window” in urine (specimen should be collected within 24-48h of use). Also specify “neutropenia” or “agranulocytosis” **and** “levamisole toxicity suspected” in the *Clinical Information*

section of the requisition. Contact your referral toxicology laboratory if more information is required.

If clinicians become aware of any more cases, public health would greatly appreciate a telephone notification giving the patient's name, date of birth, PHN, Address and phone number as we are monitoring the situation.

Advice to clients at risk should include a warning that the cocaine being sold is potentially cut with a dangerous substance that could harm their immune systems. **They should seek medical attention rapidly if they develop a fever over 38°C or have any signs of infection.** Also any skin, abscess or lung infections that appear to be developing more rapidly or are progressing more seriously may indicate an underlying acute immunodeficiency and require even more immediate treatment than usual.

Thank-you for your cooperation in this matter.

Sincerely,

(Original Signed)

James Talbot MD, Ph.D. FRCPC
Associate Medical Officer of Health