Agranulocytosis (neutropenia) associated with levamisole in cocaine in British Columbia

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Cases of agranulocytosis associated with the use of cocaine containing levamisole were identified in British Columbia in 2008 following an alert from Alberta.[1] From early 2008 to February 2011, 45 cases were reported by physicians throughout BC, including at least three deaths.

Historically, levamisole was used as an immunomodulating agent to treat some cancers, autoimmune diseases, and nephrotic syndrome, but was replaced over time by more effective drugs with less adverse effects.[2-4] Levamisole was also used as a veterinary antihelminthic agent, but has not been available in Canada for any purpose since 2005.[5] Levamisole is known to cause agranulocytosis in 3% to 10% of exposed persons and is associated with the development of cutaneous necrosis and vasculitis, often involving a purpuric eruption on earlobes and cheeks.[1,6] The US recently reported that 69% of cocaine seized at its borders contains levamisole.[7]

Public Health in BC continues to receive reports of agranulocytosis related to levamisole in cocaine. Current surveillance of this condition consists of voluntary reporting by BC physicians using a standard case report form, which is collated at the BC Centre for Disease Control (BCCDC), and review of data from the BC Coroner's Service. More cases have been reported in females (53%) and among First Nations (58%). Smoking crack cocaine (rock) is the most common route of cocaine administration identified by cases.[1] There are likely additional unreported cases; a review of Alberta laboratory data identified cases as far back as 2006, and anecdotal reports of cases have been received in BC without an associated report form.

Agranulocytosis is suspected in persons with cocaine use and signs of rapidly progressing infection (i.e., skin abscesses, pneumonia). Diagnostic testing includes complete blood count and differential to identify neutropenia. If the neutrophil count is <1.0 per 10^9 cells/L and the patient has signs of active infection, urgent hospital admission and infectious work-up with blood cultures is required. Management includes hematology referral and administration of broad spectrum antibiotics (e.g., Piperacillin/Tazobactam, Imipenem or Ceftazidime) and Filgrastim (G-CSF). Recovery generally occurs in 7 to 10 days, but close monitoring is required. Recurrence is common; neutropenia has recurred in about half of cases when re-exposed, and two cases have had seven or more episodes reported.

BCCDC is also investigating genetic markers and behavioral risk factors for the development of levamisole-associated neutropenia. Markers under investigation include the major histocompatibility complex haplotype HLA-B27, which has a strong association with other autoimmune conditions such as ankylosing spondylitis, and is thought to be a predisposing factor for the development of anti-neutrophil antibodies and subsequent neutropenia. Patients who give informed consent are asked to complete a questionnaire and provide a saliva sample for genetic-marker analysis; four age, sex, and ethnicity-matched cocaine-using controls will be recruited.

Agranulocytosis is suspected in persons with cocaine use and signs of rapidly progressing infection (i.e., skin abscesses, pneumonia).

If you suspect that one of your patients may have agranulocytosis secondary to cocaine contaminated by levamisole, please complete a provincial reporting form available at www.bccdc.ca/cocaine for both first-time and repeat episodes. General

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Dr Buxton is a physician epidemiologist and the harm reduction lead at the BC Centre for Disease Control. She is co-chair of the BC Harm Reduction Strategies and Services Committee and principal investigator of a study on pharmacogenetic interactions in cocaine users who develop neutropenia from levamisole-tainted cocaine. Ms Kuo is a federal field epidemiologist currently positioned at the BC Centre for Disease Control, Epidemiology Services. She is coordinating the study on pharmacogenetic interactions in cocaine users who develop neutropenia from levamisole-tainted cocaine. Dr Purssell is an associate professor at the University of British Columbia and the medical director of the BC Drug and Poison Information Centre, located at the BC Centre for Disease Control.

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information on agranulocytosis secondary to cocaine contaminated with levamisole and information on the study can also be found on this website.

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