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View from the front lines: An emergency medicine perspective on clostridial infections in injection drug users

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ABSTRACT

Injection drug use (IDU), specifically non-intravenous "skin-popping" of heroin, seems to provide optimal conditions for Clostridial infection and toxin production. IDU is therefore a major risk factor for wound botulism and Clostridial necrotizing soft tissue infections (NSTI) and continues to be linked to cases of tetanus. Case clusters of all 3 diseases have occurred among IDUs in Western U.S. and Europe. Medical personnel who care for the IDU population must be thoroughly familiar with the clinical presentation and management of these diseases. Wound botulism presents with bulbar symptoms and signs that are easily overlooked; rapid acquisition and administration of antitoxin can prevent neuromuscular respiratory failure. In addition to *Clostridium perfringens*, IDU-related NSTIs can be caused by *Clostridium sordellii* and *Clostridium novyi*, which may share a distinct clinical presentation. Early definitive NSTI management, which decreases mortality, requires a low index of suspicion on the part of emergency physicians and low threshold for surgical exploration and debridement on the part of the surgeon. Tetanus should be preventable in the IDU population through careful attention to vaccination status.

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1. Introduction

The association between serious infections and injection drug use (IDU) has been recognized for at least a century, and the list of infections that have now been reported in literature spans virtually the entire spectrum of infectious disease – from HIV and related opportunistic infections, to endocarditis caused by a myriad of organisms, to skin and soft tissue infections of every kind, to malaria, to diseases caused by Clostridial toxins [1–3]. IDU-related infections continue to present a substantial burden on healthcare systems worldwide. In 2011, IDUs paid 1.25 million visits to U.S. emergency departments (EDs), the majority related to heroin use, a 100% increase from 2004 [4]. Most of these visits occurred at public, inner city, safety net hospitals, with patients presenting initially to very busy EDs. For example, a handful of metropolitan counties handle 87% of all IDU-related infections in California [5]. Emergency physicians in cities like San Francisco and Oakland have become adept at recognizing and managing the diseases of IDU.

Meanwhile, beginning in the 1980's, the arrival into the Western U.S. of black tar heroin from Mexico, and its eventual market dominance, resulted in the dramatic emergence of Clostridium-related disease among IDU's [6]. Clostridial necrotizing skin and soft tissue infections (NSTIs) and wound botulism are now among the most feared and challenging problems encountered in our ED in Oakland, California. A similar increase in these diseases, beginning around the year 2000, has occurred among IDU's in Western Europe. This article reviews the diseases caused by Clostridial species that are commonly associated with IDU: NSTIs, wound botulism and tetanus. We emphasize the view from the front lines and the challenge of rapid diagnosis and treatment in the emergency department.

2. Connecting black tar heroin, "skin-popping" and clostridium

Named for its dark, sticky appearance, black tar heroin is produced primarily on volcanic hillsides of Jalisco, Mexico, and from there it is transported north and smuggled across the U.S.–Mexico border. It was initially distributed to cities in the Western U.S. where heroin use was already endemic. Black tar heroin provided the consumer a high-potency, cheap alternative to East and Central Asian heroin (so-called China White) that had previously dominated the U.S. market [7,8]. By 1990, black tar heroin dominated the heroin market west of the Mississippi River. Its arrival in cities like

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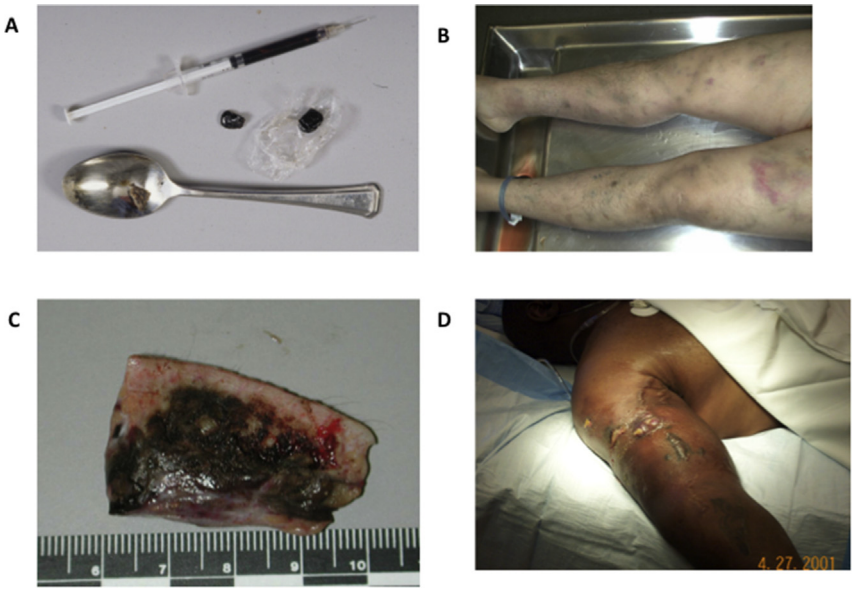

Fig. 1. A. Confiscated black tar heroin, and paraphernalia. B. Lower extremities of a patient who died of wound botulism related to black tar heroin injection. C. Cut tissue section from the patient in B, showing subcutaneous carbonaceous deposits from "skin popping" black tar heroin. D. Upper extremity NSTI due to black tar heroin injection, showing skin necrosis and extreme edema (termed the "Michelin Man sign"); note that track marks, normally depressed relative to the skin surface, are protruding outward with tense edema, and that the deltopectoral groove is also filled in with edema that has spread to the trunk; this patient died shortly after surgical debridement. Figures A–C courtesy of Dr Richard Harruff, with permission of the original publisher.

Phoenix, Los Angeles, Seattle, and San Francisco was paralleled by a spike in heroin-related ED presentations, and a doubling of heroin-related overdoses [9]. In the early 2000's, distribution of black tar heroin widened into previously heroin-naïve middleclass communities in the Eastern U.S., such as Ohio, Virginia and North Carolina, where cartels targeted existing prescription opioid addicts, dramatically undercutting the cost of drugs like oxycodone [8].

There are numerous ways that Clostridial species are hypothesized to contaminate heroin. Initial production from poppies involves boiling in acid at temperatures exceeding 150 °C, which likely eliminates any viable spores [10]. However, as black tar heroin, which is brown in color, makes its way from the site of production in Mexico to the U.S. border, it is cut with a variety of brown organic materials, which increase its weight for sale (Fig. 1). These materials – including shoe polish, wood pulp, coffegrounds, and dirt – are believed to be a major source of contamination with Clostridial spores [10]. Powdered white heroin originating from Afghanistan and Pakistan, which predominates in the European and the UK markets, is thought to be contaminated by dust during overland transport and distribution. However, descriptions of dark, sticky heroin samples also appear in reports from Europe [7,11,12]. Heroin and injection paraphernalia can be contaminated by the user in a number of ways as well. In preparation for injection, heroin is dissolved in a solvent of some kind, including saliva or lemon juice, and then heated to near boiling temperatures. This process likely destroys most bacteria other than Clostridial spores, which have been shown to survive such conditions [13,14]. As heroin is withdrawn into the syringe, it is usually filtered through cotton or similar material and users often lick the needle. A molecular epidemiology investigation of an NSTI cluster in San Francisco found the identical clone of *Clostridium perfringens* on drug paraphernalia used in black tar heroin preparation and in surgical cultures [15].

In addition to the contamination of heroin and paraphernalia with Clostridium, the practice of "skin-popping" appears to be integral to infection [10,13,16,17]. As opposed to intravenous administration, "skin-popping" refers to injection of heroin into extravenous subcutaneous tissue and muscle, typically in and around the deltoid, gluteus, and quadriceps. As venous access eventually becomes difficult due to vein sclerosis from repeated injection, users are forced to resort to "skin-popping." Injection into confined tissue compartments is thought to lead to local muscle inflammation and necrosis (Fig. 1). Additionally, subcutaneous and intramuscular injection bypasses immediate exposure to the bloodborne immunologic response, which may prevent infection after intravenous injection [13]. "Speedballing," where heroin is combined with vasoconstrictors like cocaine or methamphetamine, further decreases local blood flow to the injection site and exacerbates ischemia [18]. All of the aforementioned lead to relative anaerobic conditions that can promote spore germination and vegetative growth of Clostridial species [19,20]. "Skin-popping" is very strongly associated with wound botulism. Brett et al. reviewed 33 cases of wound botulism from 2000 to 2002 in the UK, with 100% of patients reporting "skin-popping" as a means of heroin injection [21]. Similarly, "skin-popping" was recorded in the majority of IDU-related tetanus cases in California [17]. Compared to intravenous administration, "skin-popping" is associated with a 5-fold increase in the incidence of skin and soft tissue infections, predominantly abscesses, and in the largest series of IDU-related NSTIs, cases occurred almost exclusively after "skin-popping" [22,23].

3. Tetanus

Tetanus has been clearly linked to IDU, and though far less common than wound botulism or NSTI's, it continues to be a threat in this vulnerable population. The first report of tetanus due to "the habitual injection of morphine" appeared in the *Lancet* in 1876 and since then, IDU-related cases have come to constitute an increasing proportion of total infections [24]. After black tar heroin appeared in the U.S., IDU-related tetanus cases increased from 1 per year in 1987 to 6 per year in 1997 [17]. In the most recent report on tetanus in the US from 2001 to 2008, there were a total of 233 cases, 25% in California [25]. Of the 176 patients in which IDU practices were addressed, 27 (15%) admitted to IDU, and 59% of these were Hispanic [25]. A previous report from 1987 to 1997 found that 40% of