

# Free-ranging Rocky Mountain bighorn sheep and an outbreak of inflammatory bowel disease along the Clark Fork River in Plains, Montana

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**Keywords:** *Mycobacterium avium paratuberculosis*, inflammatory bowel disease, outbreak, fecal-oral waterborne transmission, aerosolization

Nine individuals with ulcerative colitis or Crohn disease grew up or lived in Plains, Montana, a 1,200-person community adjacent to the Clark Fork River near herds of free ranging Rocky Mountain bighorn sheep. This inflammatory bowel disease outbreak is similar to others that have occurred along rivers contaminated by animal feces.

## Introduction

Over a decade ago, Fredricks and Relman<sup>1</sup> proposed that the majority of so called “autoimmune” diseases such as ulcerative colitis and Crohn disease (the two major forms of inflammatory bowel disease) are actually infectious in etiology. They based their proposal in part on the publication in the medical literature of time-space “clusters,” which are groups of individuals, whether related or not, who live near one another and develop a disease within a relatively limited time period.

Most published clusters are actually outbreaks, since “outbreak” refers to aggregations of disease that are greater than expected, while “clusters” are aggregations that are not necessarily greater than expected.<sup>2</sup> In Mankato, Minnesota,<sup>3</sup> seven of 285 contacted members of the Mankato West High School class of 1981 have Crohn disease, an “extraordinary” prevalence rate of 2,400/100,000, in contrast to nearby Olmsted County, Minnesota’s prevalence rate of 174/100,000.<sup>4</sup> In Forest, Virginia, three of an estimated 60 individuals with Crohn disease or ulcerative colitis from a community of 8,006 developed Crohn disease within a six month period, an incidence rate almost 50 times the expected rate.<sup>2</sup> In Northport, Washington a reported<sup>5</sup> 54 individuals from a community of 330 have ulcerative colitis or Crohn disease, a

combined prevalence rate of over 16,300/100,000. These three American inflammatory bowel disease (IBD) outbreaks, as well as particularly high rates of Crohn disease in Spokane, Washington in the US,<sup>6</sup> Cardiff in Wales,<sup>7</sup> Winnipeg, Manitoba in Canada<sup>8,9</sup> and Canterbury in New Zealand<sup>9,10</sup> have occurred in communities located near rivers, lakes and creeks whose surface waters are contaminated by dairy cattle and/or domesticated sheep feces.

*Mycobacterium avium* subspecies *paratuberculosis* (MAP), the cause of a chronic gastrointestinal disease in dairy cattle, domestic sheep and other animals called Johne (“Yo-knee”) disease,<sup>11</sup> is excreted in an infected animal’s feces and so is consistent with the putative microorganism linked to previously reported IBD outbreaks. MAP is the long-suspected cause of Crohn disease<sup>12</sup> and has recently been proposed as the possible etiologic agent of ulcerative colitis as well.<sup>13</sup>

While previous IBD outbreaks have been linked to dairy cattle and/or domestic sheep, the following is the first report of an IBD outbreak associated with a wild animal, the free ranging Rocky Mountain bighorn sheep.

## Findings and Discussion

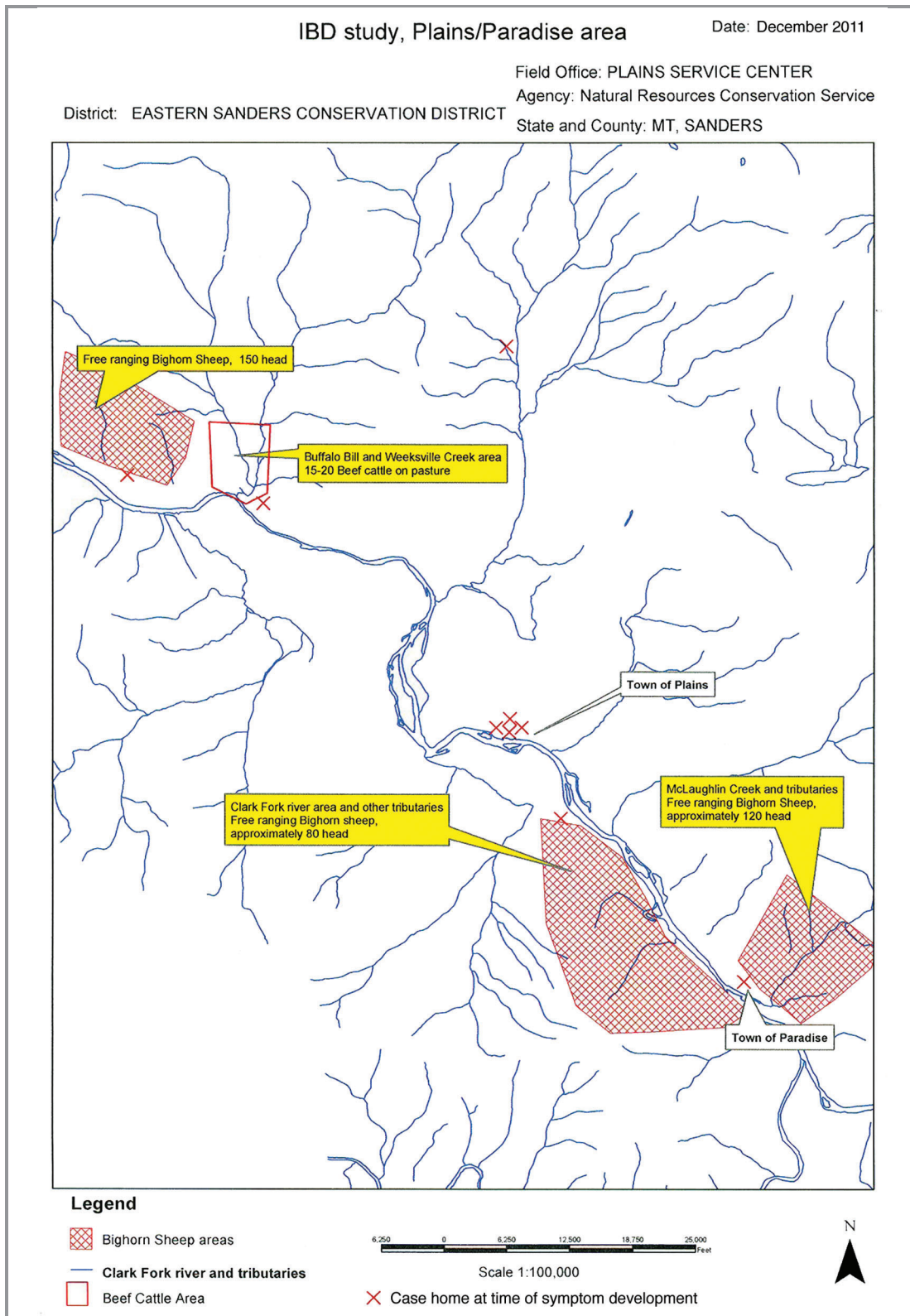
The seven Crohn disease and two ulcerative colitis cases were either born in Plains or

moved there before developing symptoms of IBD. Their average age at symptom onset was 22 y, with a range from 9 to 53 y. The first case developed symptoms in 1995, the last in 2008. Some of the cases lived in multiple homes in Plains; **Figure 1** indicates the home the case was living in at the time of symptom onset.

As with previous outbreaks, the greatly increased prevalence and incidence rates support the idea of an infectious etiology. The point prevalence rate of IBD in Plains is 9/1,200, or 750/100,000, almost double the normal prevalence rate in high incidence countries.<sup>4</sup> Two of the Crohn cases developed symptoms within a three month period at most, for an incidence rate of two Crohn disease cases/1,200/3 mo, **more than 75 times** the “expected” rate of 7.9 cases/100,000/year.<sup>4</sup>

The fact that this and previously reported IBD outbreaks as well as unusually high rates of Crohn disease have occurred near rivers, lakes and other bodies of water contaminated by a probably MAP-infected animal’s feces suggests that a possible route of transmission of MAP from an infected animal to humans is indirect fecal-oral transmission via the inhalation of MAP-contaminated aerosolized water droplets. The inhalation of MAP-contaminated water droplets as a possible route of transmission of MAP from an infected animal’s feces to humans was first proposed by Hermon-Taylor and

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Submitted: 07/30/12; Revised: 09/07/12; Accepted: 09/07/12  
<http://dx.doi.org/10.4161/viru.22121>



**Figure 1.** Map of the 1995–2008 Plains, Montana IBD outbreak. Note that all of the case homes are adjacent to the Clark Fork River or along one of its tributaries.

colleagues in 2000<sup>14</sup> to explain the ongoing outbreak<sup>15</sup> of Crohn disease in Cardiff, and in 2005 his group identified MAP in the water of the Taff River that runs through that city.<sup>7</sup> In Forest, Virginia, both the creeks that are the source of MAP-contaminated aerosolized water droplets, and the dairy cows whose manure is contaminating those creeks, are literally in several of the Forest cases' backyards.<sup>7</sup> In Northport, Washington, 400–500 small dairies were located along the Sheep Creek that runs through Northport in the 1940s, 1950s and 1960s, and the dairy barns were deliberately constructed above the creek so manure was deposited directly into it. While direct fecal-oral, rather than inhalation, is a major route of transmission of MAP from one dairy animal to another, the inhalation of MAP-contaminated aerosolized water droplets has been proposed<sup>16</sup> and is now an experimentally documented<sup>17</sup> source of bovine intestinal infection.

The aerosolization of MAP-contaminated water into small droplets capable of being inhaled and reaching human alveoli occurs in two steps, whether in outdoor or indoor environments. Indoors, MAP's resistance to chlorination,<sup>18</sup> production of and adherence to biofilms,<sup>19</sup> and adherence to both plastic and metallic water pipes<sup>20,21</sup> causes it to be concentrated in potable or drinking water.<sup>21,22</sup> Outdoors, MAP's extremely hydrophobic cell wall causes it to float to and be concentrated at the surface<sup>23</sup> of a natural body of water such as a river, lake or creek.<sup>24</sup>

Step two of the aerosolization process is the actual aerosolization of water into small jet<sup>25</sup> and film<sup>26</sup> drops that further concentrate MAP organisms. In indoor environments, the exit of water from bathroom faucets<sup>27</sup> and showerheads<sup>28</sup> and playing in baths filled with water are some of the mechanisms of water droplet aerosolization. The historically high rates of IBD in urban as compared with rural environments<sup>29</sup> as well as the reported association between Crohn disease and domestic hygiene<sup>30</sup> might not be due to the lack of exposure to a variety of enteric organisms but instead to specific exposure to highly concentrated doses of MAP spraying out of showerheads<sup>31</sup> and bathtub faucets.<sup>27</sup>

In outdoor environments,<sup>25,26</sup> precipitation, the movement of water against the creek, stream or riverbank, and playing, swimming or splashing about are some of the means by which air bubbles are created within natural bodies of water. The air bubbles then "scavenge"<sup>32</sup> MAP organisms in the bulk water and those concentrated in the surface microlayer.<sup>23</sup> The jet and film drops created by the air bubbles bursting from the water's surface again further concentrate MAP organisms.<sup>25,26</sup> MAP is a member of the MAI (*Mycobacterium avium intracellulare*) complex of microorganisms, which are preferentially aerosolized from natural bodies of water in very high concentrations.<sup>33,34</sup>

Symptom onset for four of the nine cases occurred in the summer months of June, July or August, and for another four cases in the fall months of October or November, similar to the pattern of symptom onset of acute gastrointestinal illnesses following periods of both high precipitation (spring) and low (summer) in areas with heavy livestock and thus manure density.<sup>35</sup> Precipitation is one of the mechanisms for air bubble and water droplet production and MAP organism concentration as described in step two of the aerosolization process, perhaps accounting for the increase in cases in the summer months following northern hemisphere spring rainfall. Evaporation of water from the Clark Fork River in the hot summer months further concentrates MAP in the already concentrated surface microlayer of the river as described in step one of the aerosolization process, perhaps accounting for the increase in cases in the fall months.

Dairy cattle were the first animal species described with gastrointestinal disease caused by MAP infection, and are the probable source of MAP in the Forest, Virginia<sup>2</sup> and Northport, Washington<sup>5</sup> American IBD outbreaks. There are, however, no dairy cattle within a 70-mile radius of Plains. MAP is known to cause gastrointestinal disease in a wide variety of animal species other than dairy cattle.<sup>11</sup> In this outbreak, the two possible sources of MAP are a single small beef cattle herd, and three large herds of free ranging Rocky

Mountain bighorn sheep (Fig. 1). Given the small size of the nearby beef herd (less than 20 head) and the low prevalence of MAP infection in beef cattle,<sup>36</sup> the bighorn sheep are the likely source of MAP contaminating the Clark Fork River. Such sheep are known to be infected with MAP, to develop gastrointestinal disease and to shed MAP in their feces.<sup>37–40</sup>

Although MAP can be identified in human and Bighorn sheep blood,<sup>40,41</sup> tissue<sup>37,38,42</sup> and feces<sup>39,43</sup> and in droplets aerosolized from natural bodies of water,<sup>33</sup> the author suffers from catastrophic and irreversible complications of Crohn disease<sup>44</sup> and is unable to further evaluate this outbreak. Attempts by the families in this and the Forest, Virginia IBD outbreaks to elicit evaluation and investigation by state public health authorities and the United States' Center for Disease Control and Prevention have been met with either silence or repeated and pointed refusal. In private correspondence, MAP researchers have expressed their frustration with the refusal of IBD-related organizations and government agencies to fund any research related to MAP. One prominent researcher has alluded to this difficulty, having to resort to "donations from people suffering from Crohn disease, their families and friends."<sup>9</sup> The publication of yet another American IBD outbreak will hopefully begin to encourage a reappraisal of public health and research priorities.

#### Acknowledgments

The author is indebted to the cases and their families who brought their outbreak to her attention and gave written permission to be included in this report. She is also most grateful for the assistance of an employee of the United States Department of Agriculture's office in Plains, Montana for the preparation of and information contained in Figure 1, and, as always, Dr Dodie Ruzicki and the librarians of Providence Sacred Heart Medical Center and Children's Hospital's Health Sciences Library in Spokane, WA for the references. The author declares that no competing interests exist. The author received no funding for this case report.

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