Human Cutaneous Anthrax, Georgia 2010–2012

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We assessed the occurrence of human cutaneous anthrax in Georgia during 2010–2012 by examining demographic and spatial characteristics of reported cases. Reporting increased substantially, as did clustering of cases near urban centers. Control efforts, including education about anthrax and livestock vaccination, can be directed at areas of high risk.

Anthrax, a zoonosis caused by the bacterium *Bacillus anthracis*, is associated with rural areas or agricultural production (*1–3*). Human infections often result directly from contact with infected livestock or contaminated animal materials (*2*). Although several countries have implemented successful control strategies, anthrax remains a re-emerging threat to public health in areas with weak health systems. After the Soviet Union collapsed, the country of Georgia underwent funding cuts to public health and animal health infrastructure, limiting disease management (*2*). Human anthrax cases more than tripled in Georgia after Soviet governance discontinued; 118 cases were reported during 1991–1996, compared with 36 during 1985–1990 (*4,5*). Recent reports indicating a worsening anthrax situation in Georgia have raised concern about spread of anthrax to new areas (*5,6*). To assess this situation, we analyzed demographic risk factors and characterized spatial patterns of human cutaneous anthrax (HCA) in Georgia.

The Study

Anthrax is nationally reportable in Georgia. We analyzed passive surveillance data on HCA cases reported to the National Center for Disease Control and Public Health (Tbilisi, Georgia) during 2010–2012. Case investigation forms included patients' community of residence, age, and sex. Self-reported source of infection was ascertained from categorical responses that included butchering/

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slaughtering cattle, handling/preparing meat, performing field work/harvesting crops, processing hair/wool, receiving an insect bite, unknown, or other. We also obtained information about regional-level anthrax cases in livstock (www.oie.int/wahis_2/public/wahid.php/disease information/statusdetail). HCA cases and incidence per million persons were plotted over time with livestock cases. To estimate changes in HCA risk over time, we compared data for the study period with data for 2007–2009 by using a cumulative incidence ratio (total cases/median year population). We calculated incidence risk ratios for demographic characteristics by using a negative binomial regression (online Technical Appendix, wwwnc.cdc.gov/eid/article/20/2/pdfs/13-0522-Techapp1.pdf).

Data were anonymized and aggregated to each case-patient's community of residence and mapped in a geographic information system. We extrapolated current population from the 2002 census using the United Nations medium variant population growth projections (http://data.un.org/). Cumulative incidences per 10,000 population were calculated for each community (total cases/median year population). National and community population data were obtained from GeoStat (http://geostat.ge).

We adjusted for community population heterogeneity using Empirical Bayes smoothing estimates of the cumulative incidence (online Technical Appendix). Kernel density estimation was used to map the cumulative incidence risk/km^2 (online Technical Appendix). To identify community-level HCA spatial clustering, we used the Poisson model in SaTScan (*7*) with a maximum cluster size of 25% of the population at risk. We compared the proportion of urban and rural communities inside and outside clusters using a χ^2 analysis (PROC FREQ, SAS Institute, Cary, NC, USA).

During 2010–2012, a total of 251 HCA cases and 74 livestock cases (38 cattle, 1 pig, 4 sheep/goats, 1 horse) were reported (Figure 1). HCA cases peaked in 2012 (142 cases), corresponding to a national incidence of 31.7 per million population (95% CI 28.4–36.1). Compared with 2007–2009 (133 cases), the period studied had a higher risk for HCA (cumulative incidence ratio 1.89 [95% CI 1.64–2.33], p<0.01).

Cases occurred predominantly in males (209 [84%]) (Table 1). Butchering/slaughtering cattle as a source of infection was more common among male patients (143 [68%]); processing/handling meat was more common among female patients (28 [68%]). Case-patients' median age was 43 years [range 5–79]. The adjusted incidence risk ratios from the negative binomial model showed a stronger association of risk in males (4.95 [95% CI 2.91–8.42]) than in females (Table 2). Persons 50–64 years of age were at greater risk than were persons in all other age groups.
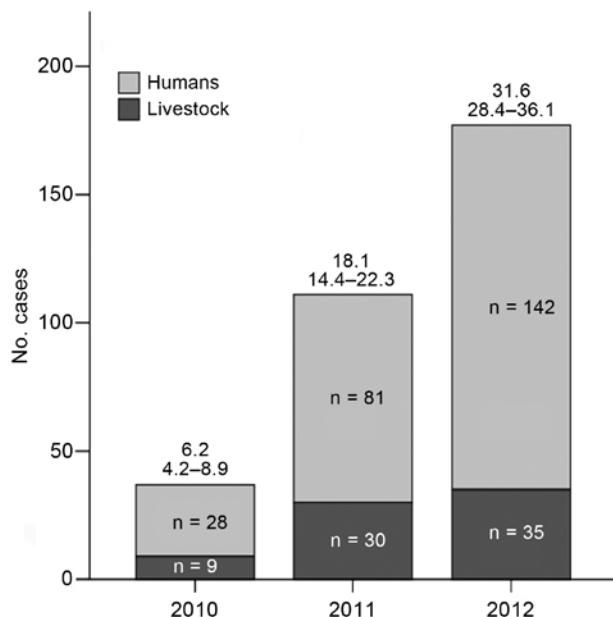
Figure 1. Total number of human cutaneous anthrax cases (light gray) and livestock cases (dark gray), Georgia, 2010–2012. Incidence rates (IRs) (95% CIs) of human cutaneous anthrax per million population are displayed above the bars.

Risk did not differ between case-patients who processed/handled meat and those who slaughtered/butchered cattle.

Empirical Bayes smoothed incidence per 10,000 population ranged from 0.11 (95% CI 0.03–0.37) to 213.8 (95% CI 72.8–552.6) (Figure 2, panel A). The kernel density analysis identified a higher risk per squared kilometer in the southeast and west (Figure 2, panel B). We identified 3 spatial clusters of high risk; the clusters comprised 58 communities with 197 cases (Figure 2, panel C). Cumulative incidence inside the clusters was 12.8/10,000 population compared with 0.96/10,000 population outside the clusters. The proportion ($\chi^2 = 0.65$, p = 0.4) of urban and rural communities (22 and 36, respectively) within clusters did not differ from the proportion outside clusters (urban: 14; rural: 24). Clusters 1 and 2 in the southeast bordered

the densely populated urban area of the capital (Tbilisi) and were associated with grazing lands, whereas cluster 3 bordered the urban area of Poti in the west and was associated with a higher percentage of croplands.

Conclusions

Despite an apparent decline in HCA cases worldwide (8), incidence in Georgia has increased and is now comparable with that in Turkey, where the disease is hyperendemic (1,9,10). Our analysis identified clusters of communities that were of historical importance for HCA risk and new communities that represent areas of (re)emergence (6).

Our findings indicate that HCA cases were concentrated within specific areas associated with agriculture and in close proximity to urban centers (Figure 2), consistent with research linking urban livestock trading centers and markets to outbreaks and higher rates of HCA (5,9–11). Sick and dying animals are often slaughtered and brought to market quickly to mitigate economic losses, thereby exacerbating exposure risk while limiting livestock reporting (10,11). HCA is primarily associated with rural, agrarian areas (2,3,12), but we found no difference in the proportion of urban and rural communities in high-risk clusters. This association with urban zones suggests reliance on these areas for commerce, coupled with increased agricultural employment from 25% of the population in 1990 to ≈55% in 2010 (5,13). One hypothesis is that contaminated meat is brought into urban areas and sold at informal meat markets that because of fiscal constraints have little to no regulation.

Cases were predominantly linked to contact with infected livestock or meat, as observed elsewhere (2,3,9,11). Field work was a self-reported source of infection in 27 (10.7%) cases. This risk factor is not well documented and might reflect recall bias or unwillingness to admit to slaughtering infected animals. Our findings that males were at higher risk than females for HCA, as reported elsewhere (2,14) might reflect occupational exposures or gender roles, with males slaughtering/butchering livestock and

Table 1. Characteristics of human cutaneous anthrax patients, Georgia, 2010–2012				
	Male case-patients		Female case-patients	
Characteristic	No., n = 209	Population*	No., n = 42	Population*
Age, y				
5–19	14	522,736	2	506,785
20–34	57	458,998	8	480,276
35–49	62	443,820	12	502,732
50–64	61	292,713	15	361,370
65–79	15	196,171	5	286,839
Self-reported infection source				
Slaughtering cattle	143		3	
Processing meat	39		28	
Field work/sowing and harvesting crops	20		7	
Unknown	7		3	

*Population estimates were obtained from the Georgian State Statistical Office (GeoStat, http://geostat.ge) and are based on median year population totals for the study period.

Table 2. Results of the negative binomial regression model examining risk factors for human cutaneous anthrax, Georgia

Patient characteristic	IRR*		95% CI†	p value
	Univariate	Adjusted		
Age, y				
5–19	0.12	0.11	0.05–0.26	<0.01
20–34	0.57	0.46	0.23–0.91	0.03
35–49	0.65	0.58	0.30–1.14	0.11
50–64	Referent	Referent		–
65–79	0.37	0.36	0.16–0.78	0.01
Sex				
F	Referent	Referent		–
M	5.75	4.95	2.91–8.42	<0.01
Self-reported infection source				
Slaughtering/butchering cattle	Referent	Referent		–
Processing/handling meat	0.45	0.75	0.40–1.39	0.36
Field work/sowing and harvesting crops	0.18	0.26	0.13–0.51	<0.01
Unknown	0.07	0.09	0.04–0.20	<0.01

*χ^2 goodness-of-fit test indicated the model fit the data (df = 31, χ^2 = 40.71, p = 0.11). IRR, incidence risk ratio.
†Wald 95% CIs.

females more involved in preparing meat (*14*). In contrast, no gender differences were reported in Turkey or Kazakhstan (*3,9*). Although age was not a risk factor in other regions (*2,3*), persons 50–64 years of age in this study were at higher risk for infection (Table 2), reflecting changing sociocultural practices related to an agrarian lifestyle.

Although the true cause of the increase in HCA cases is unknown, it is probably due to a combination of factors
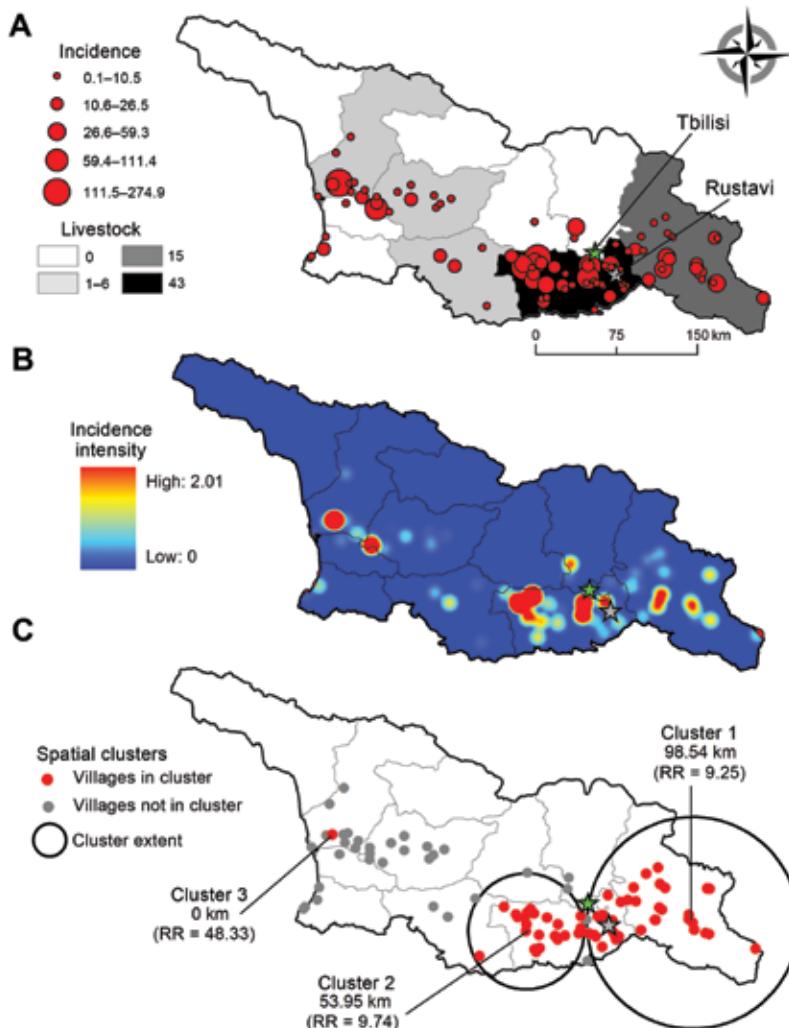

Figure 2. A) Empirical Bayes Smoothing cumulative incidence (per 10,000 population) of human cutaneous anthrax at the community level, Georgia, 2010–2012. Green star indicates the location of the capital, Tbilisi; gray star indicates the fourth most populous city, Rustavi. The total number of livestock cases during the study period is shown by region. B) Risk surface representing the estimated smoothed cumulative incidence per square kilometer. C) Spatial clustering of human cutaneous anthrax cases as determined by using SaTScan (*7*). RR, risk ratio.

related to decreased public health funding and agricultural reform resulting in a shift from collectivization to private ownership (*1,5,13*). These factors, coupled with limited veterinary control and the cessation of compulsory livestock vaccination, have played plausible roles in the increased incidence of HCA. Livestock cases were out of sync temporally and spatially with human cases, indicating anthropocentric reporting or high incidence from relatively few animals, although differences in the aggregation of livestock cases limit the inference of spatial synchrony. Controlling HCA requires controlling the disease in livestock (*1,2,9*) and highlights the need for a One Health approach. Our findings can be used to formulate public health interventions aimed at controlling anthrax in livestock and increasing awareness of the disease, particularly in urban areas. Given the limited resources available, future efforts should focus on high-risk areas for livestock surveillance and control, such as targeted vaccination campaigns (*15*).

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Technical Appendix

Statistical Methods

Negative Binomial Regression

Risk factors for human cutaneous anthrax (HCA), including age, gender, and source of infection, were identified by using a generalized linear model (GLM) regression. Because the data comprised cases stratified by demographic characteristics (Table 1), a count model was used to calculate the incident risk associated with each variable. A GLM with a negative binominal distribution was chosen to calculate incidence risk ratios in SAS v9.2 (SAS Institute, NC, USA; PROC GENMOD). Due to overdispersion in the number of anthrax cases (ratio of the mean/variance was >1) a negative binomial distribution was selected over a Poisson distribution (*1*). The underlying population within each strata of the age groups was adjusted for using the log of the population as an offset in the model. Incidence risk ratios were derived for each variable by exponentiation of the GLM model coefficients.

Empirical Bayes Smoothing

Cumulative incidence per 10,000 population (total cases/median population) were mapped at the community level by using an adjustment for population heterogeneity. Empirical Bayes Smoothing (EBS) in the GeoDa software package (ASU, AZ, USA) (*2*) can be used to adjust for instability in risk estimates caused by small sample sizes and variance in the distribution of cases and the population. The EBS method can be implemented when the numerator data total <3 cases or denominator population data are $\leq$800, which was the situation in this analysis (*3*). EBS cumulative incidence estimates are derived by using information from the overall study area population mean and the crude cumulative indigence rates. Communities with small sample populations are then adjusted toward the overall mean, and communities with large sample populations undergo very little adjustment (*3*).

Kernel Density Estimation

Kernel density estimation was used to visualize the spatial distribution of cumulative incidence per km^2. Kernel density estimation is a technique for calculating the weighted density of an event over a gridded surface within a kernel, or spatial filter (*4*). Kernel density estimation was performed with the Spatial Analyst Extension for ArcGIS 10. ArcGIS employs the quadratic kernel function described in Silverman (*5*), p. 76, equation 4.5:

$$f(x) = \frac{1}{nh} \sum_{i=1}^{n} K\left(\frac{x - X_i}{h}\right)$$

Where *h* is the bandwidth, *x-Xi* is the distance to each village with anthrax *i*. *K* is the quadratic kernel function, which is defined as

$$K(x) = \frac{3}{4}(1 - x^2), |x| \leq 1$$

$$K(x) = 0, x > 1$$

This function was employed to estimate HCA densities using cumulative incidence as the weight. We chose a bandwidth (kernel) of 9.89 km with an output cell size of $\approx$1 km^2. The resulting output was a map surface representing the cumulative risk for HCA across the country per 1 km^2.

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