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Human anthrax outbreak associated with livestock exposure: Georgia, 2012

A. NAVDARASHVILI[1], T. J. DOKER[2,3]*, M. GELEISHVILI[4], D. L. HABERLING[5], G. A. KHAROD[3], T. H. RUSH[4,6], E. MAES[4,6], K. ZAKHASHVILI[1], P. IMNADZE[1], W. A. BOWER[3], H. T. WALKE[3], S. V. SHADOMY[3] AND the Anthrax Investigation Team†

[1] *Georgia National Center for Disease Control and Public Health, Georgia Ministry of Health, Tbilisi, Georgia*
[2] *Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, GA, USA*
[3] *Bacterial Special Pathogens Branch, Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, GA, USA*
[4] *South Caucasus Field Epidemiology and Laboratory Training Program, Tbilisi, Georgia*
[5] *Division of High Consequence Diseases and Pathology, Centers for Disease Control and Prevention, Atlanta, GA, USA*
[6] *Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, USA*

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SUMMARY

Human anthrax cases reported in the country of Georgia increased 75% from 2011 ($n = 81$) to 2012 ($n = 142$). This increase prompted a case-control investigation using 67 culture- or PCR-confirmed cases and 134 controls matched by residence and gender to investigate risk factor (s) for infection during the month before case onset. Independent predictors most strongly associated with disease in the multivariable modelling were slaughtering animals [odds ratio (OR) 7·3, 95% confidence interval (CI) 2·9–18·1, $P < 0·001$] and disposing of dead animals (OR 13·6, 95% CI 1·5–119·8, $P = 0·02$). Participants owning or working with livestock ($n = 131$) were additionally interviewed about livestock management practices during the previous 6 months: 53 (44%) of 121 respondents vaccinated livestock against anthrax; 19 (16%) of 116 moved livestock >1 km; 15 (12%) of 125 had sick livestock; and 11 (9%) of 128 respondents reported finding dead livestock. We recommend joint public health and veterinary anthrax case investigations to identify areas of increased risk for livestock anthrax outbreaks, annual anthrax vaccination of livestock in those areas, and public awareness education.

Key words: Anthrax, bacterial infections, control, epidemiology, zoonoses.

INTRODUCTION

Anthrax is a zoonosis caused by the Gram-positive spore-forming bacteria *Bacillus anthracis*. The spores can remain viable in soil for decades, contributing to disease persistence [1]. Anthrax primarily occurs in herbivorous wildlife and livestock that ingest *B. anthracis* spores while grazing [2]. Biting flies and blowflies may serve as mechanical vectors [3, 4]. Human anthrax is primarily dependent on exposure to infected animals, their carcasses, or to products from infected animals (e.g. meat, wool, hides) [5]. Three primary forms of anthrax are recognized in

* Author for correspondence: Dr T. J. Doker, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop A-30, Atlanta, GA 30333, USA
(Email: thomas.doker@gmail.com).
† Members of the Anthrax Investigation Team are given in the Appendix.

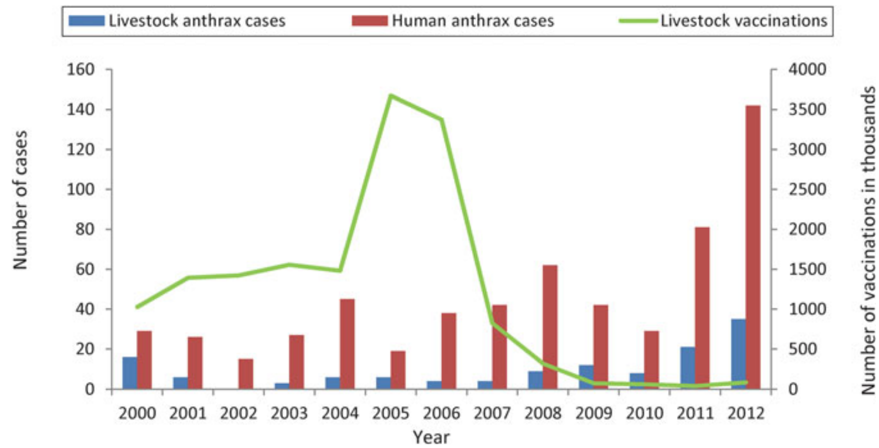

Fig. 1. Number of human and anthrax livestock cases, and number of livestock anthrax vaccinations by year, Georgia, 2000–2012. (*Source*: Georgia National Center for Disease Control and Public Health and Georgia National Food Agency.)

humans: cutaneous, gastrointestinal, and inhalation. Of these, cutaneous anthrax is the most common, comprising 95–99% [5, 6] of an estimated 2000–20 000 human anthrax cases occurring annually worldwide [7]. Anthrax is endemic in Central and Southwestern Asia, Southern and Eastern Europe, and West Africa [8]. Outbreaks frequently occur during hot, dry conditions following heavy rains and flooding, or following rains ending a period of drought [2, 9, 10]. Control of anthrax primarily depends on vaccination of susceptible livestock; surveillance, rapid identification, and treatment of affected animals; quarantine of impacted premises; prevention of animal access to contaminated pastures or feed; and appropriate disposal of infected carcasses and decontamination [2, 10].

Anthrax is considered endemic in Georgia. A 1995 law required the prevention of epizootic diseases in Georgia, which included mandatory livestock anthrax vaccinations; in 2007, responsibility shifted from Georgia National Food Agency (NFA) veterinarians vaccinating livestock annually to livestock owners contracting private veterinarians to provide anthrax vaccinations. Between 2000 and 2012, the NFA reported 120 livestock anthrax cases; the number of livestock cases increased threefold between 2010 and 2012 (Fig. 1). However, it is assumed that livestock cases are greatly underreported. Of those livestock cases reported in the OIE WAHID database [11] from 2007 to 2012, 65% were from Kvemo Kartli and Kakheti, two adjoining regions in Eastern Georgia; in 2012, according to the Geostat database [12], Kvemo Kartli and Kakheti had 40% of all livestock in Georgia.

Between 2000 and 2012, 597 human cases were reported to the Georgia National Center for Disease Control and Public Health (NCDC); of these, 86% were reported from Kvemo Kartli and Kakheti. From 2000 to 2010, the annual number of human cases in Georgia ranged from 15 to 62. The number of cases increased from 28 in 2010 to 81 in 2011, and increased again by 75% to 142 in 2012. Seventy-seven cases reported in 2012 (up to July) prompted an epidemiological investigation of anthrax in Georgia in order to characterize the outbreak.

METHODS

Descriptive epidemiology and control strategies

At the start of the investigation in August 2012, a line listing of cases by region, district, settlement, and date was used for planning. At the end of 2012, all NCDC confirmed and probable human anthrax cases for the year were enumerated, demographic data were extracted, and an epidemic curve was plotted. Cases meeting the following case definitions were identified in the electronic integrated disease surveillance system (EIDSS):

- *Confirmed case*: clinically compatible illness with culture and identification of *B. anthracis* from clinical specimens, or by evidence of *B. anthracis* DNA by PCR in clinical specimens collected from a normally sterile site (e.g. blood or cerebral spinal fluid) or from a lesion (skin, pulmonary, reticuloendothelial, or gastrointestinal).
- *Probable case*: clinically compatible illness that does not meet the confirmed case definition, but is

epidemiologically linked to a documented anthrax environmental exposure.

Livestock anthrax cases reported to the OIE WAHID database [11] were added to the epidemic curve. A one-sample *t* test was used to compare 2012 case counts to counts from previous years. Interviews were conducted with NCDC and NFA personnel to determine medical and veterinary outbreak response measures.

Case-control investigation

In order to provide data on exposures and risks associated with human anthrax, a case-control investigation was planned for the locations with the highest human anthrax incidence. The activity was conducted as a 1:2 matched case-control investigation, specifically investigating exposure and risk factors during the 1-month period prior to the onset date for the case associated with each case-control triplet. Cases and controls were limited to persons aged $\geqslant 18$ years. Controls were matched by place of residence (within 250 m of the case's residence) and gender, and were recruited by random selection from the closest households to the case's household in which potential subjects were present. In the instance of a refusal, the next household or potential subject was selected until a control was recruited. Gender matching was used due to the possibility of over-selecting females because most males were away from home during working hours.

The case-control investigation questionnaire addressed human, livestock, and environmental risk factors that may have contributed to the occurrence of human anthrax. Concerns were raised by various ministry staff regarding perceived risk from soil exposure, so soil-specific exposure questions were added. Occupational exposures assessed included livestock-related occupations (herder/shepherd, farmer/rancher, livestock worker, veterinarian, slaughterhouse worker, or butcher); other occupations assessed were housewife and student. Slaughter of livestock was considered a risk factor if respondents participated in slaughter of any livestock, whether or not their own.

Cross-sectional assessment

Following completion of the case-control questionnaire, respondents identified as owning or working with livestock were asked to participate in the cross-sectional survey. The objectives were to identify animal management practices or exposures associated with the occurrence of anthrax in livestock and to assess the history of anthrax in the respondent and possible livestock illness or losses which were not previously identified as due to anthrax. All questions addressed the 6 months prior to the interview date.

Questionnaire/interview procedures

The questionnaires were translated into the major languages used in the regions (Georgian, Azeri, Russian). Interview teams were trained on the investigation protocol, informed consent procedures, and questionnaire, and were provided colour pictures of cutaneous anthrax lesions to assist with interviews. Teams included native Azeri language speakers for interviews in villages with primarily Azeri-speaking populations.

Anthrax cases occurring in Kvemo Kartli and Kakheti from April to October 2012 were considered for recruitment. For case-patients not at home at the time of the interview visit, we either arranged meetings or conducted phone interviews. Potential controls were limited to those who were at home during the time of the interview visit; demographic data and addresses of the cases were known and controls could be recruited in the associated neighbourhoods.

Data management and analysis.

Epi Info v. 7.1 (CDC, USA) was used for data management. Data were independently double-entered and validated. All data collection instruments were identified in NCDC and CDC records by unique project ID numbers only. SAS v. 9.3 (SAS Institute Inc., USA) was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) to compare risk factors of cases and controls using conditional logistic regression. Multivariable model selection utilized backward selection on all combinations of the most significant variables from univariate analysis, accounting for multicollinearity and minimizing missing strata to $< 10\%$.

Ethical review

The investigation protocol was reviewed by the NCDC and CDC National Center for Emerging and Zoonotic Infectious Diseases, in accordance with institutional review policies. The protocol was determined to be non-research under 45 CFR 46·102 (d), and therefore did not require IRB review.

Fig. 2. Human anthrax incidence (per 100 000 population) by region, Georgia, 2012 (http://www.geostat.ge/).

RESULTS

Descriptive epidemiology and control strategies

In 2012, 110 confirmed and 32 probable human cutaneous anthrax cases were reported (Table 1). The majority of cases occurred in Kvemo Kartli and Kakheti and corresponded to incidences of 17·8 and 7·6 cases/100 000, respectively (Fig. 2). The case count in Kvemo Kartli and Kakheti was significantly greater than the average count seen in the previous 12 years in both regions (17·1 and 4·4, respectively; $P <$ 0·001). Most cases were male and aged between 20 and 59 years. The median age for all cases was 41 years (range 5–75 years). Cases started to increase in April, peaking in June and again in October (Fig. 3). Thirty-five livestock anthrax cases – including 31 cattle, three sheep or goats, and one horse – were reported to the OIE WAHID database [11] in 2012, with cases also peaking in June and October (Fig. 4).

Interviews with NCDC and NFA personnel revealed that initial livestock investigation and control strategies were constrained by lack of resources. NCDC, NFA, and the laboratory of the Ministry of Agriculture reported surveillance data to a common

Table 1. *Demographic characteristics of human anthrax cases reported in 2012 in Georgia*

Characteristic	*n*	%
Sex		
Male	119	84
Female	23	16
Region		
Kvemo Kartli	91	64
Kakheti	31	22
Tbilisi	9	6
Samegrelo Zemo Svaneti	4	3
Imereti	3	2
Ajara	2	1
Guria	1	1
Mtskheta Mtianeti	1	1
Age group, years		
<20	7	5
20–29	29	20
30–39	26	18
40–49	33	23
50–59	32	23
>59	15	11
Total	142	100

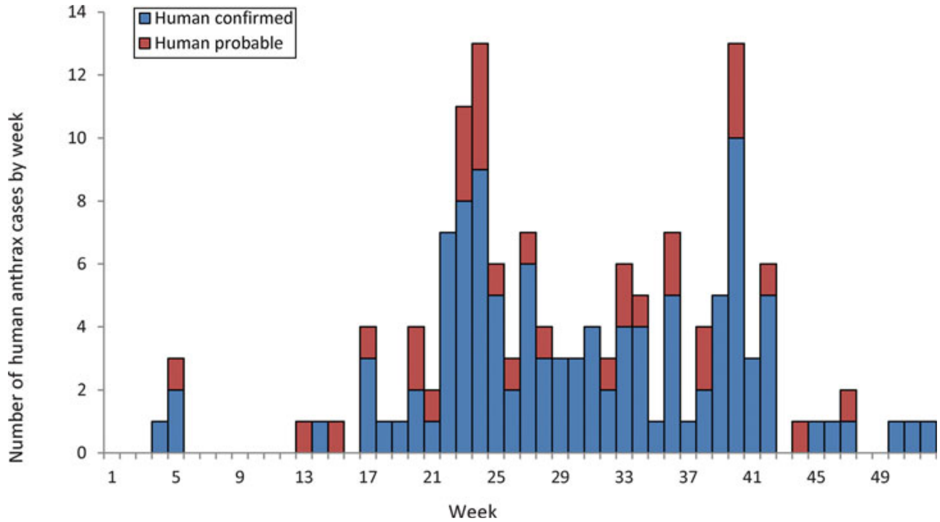

Fig. 3. Human anthrax case numbers (confirmed and probable) by week ($n = 142$), Georgia, 2012. (*Source*: data reported in the electronic integrated disease surveillance system to Georgia National Center for Disease Control and Public Health.)

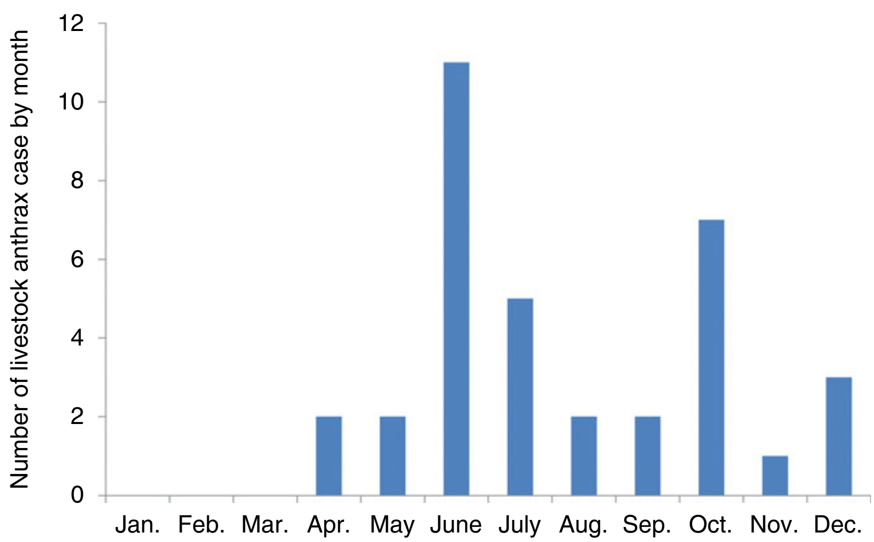

Fig. 4. Confirmed livestock cases by month, Georgia, 2012. (*Source*: data reported in OIE WAHID database [11].)

electronic system; however, data were not actively shared between human and livestock health authorities. Initial focus on soil exposures as a potential cause for human cases limited the implementation of livestock anthrax control programmes during the initial outbreak response. An ongoing national cattle identification and foot-and-mouth disease vaccination campaign delayed the start of a national cattle anthrax vaccination response programme until November 2012. During our investigation, awareness literature including prevention recommendations was distributed to neighbours around each case. Television alerts commenced in September 2012 and continued into 2013.

Case-control investigation

A total of 67 case-patients and 134 controls were enrolled in the case-control investigation; 82% ($n = 55$) of cases were confirmed, and 18% ($n = 12$) probable. The mean age of cases was 42 years (range 18–72 years), and that of controls 46 years (range 18–75 years). Cases and controls were matched on gender and region, and similar in nationality and age groups (Table 2). The majority were male and from Kvemo Kartli. Most participants were Azerbaijani or Georgian.

Individually analysed risk factors for developing anthrax are given in Table 3. The risk factors most strongly associated with case-patients were caring for

Table 2. *Characteristics of 2012 anthrax case-control investigation participants, Georgia*

Characteristic	Cases *n*	Cases %	Controls *n*	Controls %	OR (95% CI)	*P* value
Sex*						–
Male	57	85	114	85	–	
Female	10	15	20	15	–	
Region*						–
Kvemo Kartli	55	82	110	82	–	
Kakheti	11	16	22	16	–	
Tbilisi	1	1	2	1	–	
Nationality						0·6
Azeri	42	63	79	59	3·2 (0·3–36·6)	
Georgian	24	36	50	37	Reference	
Other†	1	1	5	4	Undefined	
Age group, years						0·3
18–34	23	34	36	27	Reference	
35–49	23	34	42	31	0·8 (0·4–1·6)	
⩾50	21	31	56	42	0·5 (0·2–1·2)	
Total	67	100	134	100		

OR, Odds ratio; CI, confidence interval.
* Cases and controls matched on sex and region; therefore, odds ratios are not reported.
† Other nationalities included Greek and Ukrainian.

sick livestock (OR 24·6, 95% CI 3·2–188·1, $P = 0{\cdot}002$) and disposing of dead livestock (OR 18·1, 95% CI 2·3–142·0, $P = 0{\cdot}006$). Being part of households that owned animals; slaughtering or skinning livestock; having livestock-related occupations; or participation in livestock care, including herding and removal of animal waste or dirty bedding, were associated with disease. Participation in livestock slaughter included five subcategorized activities, of which none individually were significantly associated with disease. Cases were more likely to slaughter their own livestock. Cases were also more likely to have owned cattle, horses, goats, or dogs than controls, and were less likely to report insect bites (Table 3).

Having contact with or helping to prepare livestock products (e.g. meat, skin, leather, bones) was associated with disease; however, no individual type of livestock origin product was significantly associated with disease. Eating meat from one's own farm was associated with disease while buying meat from a butcher's shop was protective. No prepared meat dish or cooking preference was associated with disease and no meat handling activities were significantly associated. Consuming raw or undercooked meat was not associated with disease, nor was the source of meat or location the meat was consumed.

Despite original concerns raised that disease was due to contact with contaminated soil, work with soil near livestock burial sites or work with soil at other locations including agricultural farm work were not associated with disease.

The independent predictors that remained most strongly associated with disease in the multivariable model were slaughtering animals (OR 7·3, 95% CI 2·9–18·1, $P < 0{\cdot}001$) and disposing of dead animals within the month prior to case onset (OR 13·6, 95% CI 1·5–119·8, $P = 0{\cdot}02$).

Cross-sectional assessment

From the pool of 201 case-control participants, 131 (65%) were eligible for enrolment in the cross-sectional assessment and all elected to participate (Table 4). Less than half of respondents reported vaccinating their livestock for anthrax in the previous 6 months. Of those who reported not vaccinating their animals for anthrax, one-third stated that they did not know about anthrax vaccination for their animals, and one-quarter stated they could not afford the vaccine; the response rates for these questions were low (22% and 24%, respectively). Other findings indicated that few of the respondents moved livestock >1 km from where they were pastured the day of the interview. Those respondents reporting sick animals also mostly reported anthrax-related symptoms, such as acute illness and/or head or neck swelling and

Table 3. *Evaluation of potential risk factors for anthrax in case-control investigation participants in the 1 month prior to case onset date, Georgia, 2012*

	Cases		Controls				
Risk factor	*n*	%	*n*	%	OR*†	95% CI	*P* value
Livestock-related occupations‡	26	48	24	25	**4·0**	**1·5–10·0**	**0·005**
Household animals	53	79	67	51	**7·2**	**2·7–19·1**	**<0·001**
Cattle	49	74	60	45	**5·5**	**2·4–12·9**	**<0·001**
Horse	15	26	9	7	**6·0**	**2·0–18·5**	**0·002**
Sheep	17	28	20	16	2·2	1·0–5·2	0·06
Goat	9	16	7	6	**3·3**	**1·1–10·0**	**0·03**
Dog	35	59	39	31	**4·6**	**2·0–10·4**	**<0·001**
Livestock care	47	70	61	47	**3·8**	**1·8–8·2**	**<0·001**
Herding	31	48	43	34	**3·2**	**1·4–7·2**	**0·004**
Cleaning§	37	61	54	43	**3·0**	**1·4–6·4**	**0·005**
Milking	15	25	29	23	1·5	0·6–3·8	0·4
Shearing	10	17	14	11	1·9	0·8–4·7	0·2
Care for sick livestock	16	25	6	5	**24·6**	**3·2–188·1**	**0·002**
Sell sick livestock	5	11	5	6	5·8	0·6–53·6	0·1
Kill/dispose of carcass	6	14	8	11	0·9	0·2–3·9	0·9
Slaughter or skin livestock	28	44	16	13	**7·0**	**2·9–17·2**	**<0·001**
Dispose of dead livestock	11	17	3	2	**18·1**	**2·3–142·0**	**0·006**
Exposed to livestock with suspected anthrax	59	92	127	97	0·3	0·1–1·5	0·1
How owner would treat sick livestock							
Owner treated	10	22	19	23	1·2	0·5–3·4	0·7
Veterinarian treated	29	63	54	66	0·9	0·4–2·2	0·9
Slaughter own livestock	27	42	29	25	**2·9**	**1·3–6·6**	**0·01**
Activities during livestock slaughter							
Holding animal down	21	81	26	93	0·2	0·03–2·2	0·2
Gutting	24	96	25	89	2·6	0·3–25·2	0·4
Killing	23	88	27	96	1·0	0·06–16·0	1·0
Skinning	24	92	24	92	2·0	0·2–22·1	0·6
Witnessing within a 10 m radius	7	33	9	33	0·3	0·03–2·7	0·3
Wear overalls or apron	3	60	6	46	Undefined		1·0
Reason no protective equipment used							
Not aware protective equipment needed	13	76	22	81	0·7	0·1–5·2	0·7
Normally does not use protective equipment	15	65	10	38	0·3	0·03–2·5	0·3
Meat handling activities							
Cutting	32	49	49	40	1·6	0·8–3·2	0·2
Preparing for cooking	21	34	45	37	0·8	0·4–1·7	0·6
Moving	29	45	40	33	2·1	1·0–4·2	0·05
Cooking	17	27	45	36	0·6	0·3–1·2	0·2
Drying	6	10	14	12	0·8	0·3–2·3	0·7
Eating	44	69	94	76	0·6	0·3–1·2	0·2
Covered injury handling meat	3	7	17	28	0·2	0·05–1·1	0·06
Meat sources							
Own farm	21	36	24	21	**3·5**	**1·3–9·4**	**0·01**
Butcher's shop	31	52	82	67	**0·4**	**0·2–0·9**	**0·03**
Grocery	10	20	22	19	0·7	0·2–2·3	0·6
Meat market	25	47	61	52	0·8	0·4–1·7	0·5
Neighbour	13	28	18	17	2·5	0·7–8·4	0·2
Mobile meat seller	8	16	18	16	0·7	0·2–2·3	0·6
Consumed raw or undercooked meat							
Source of meat							
Consumed cattle (beef)	13	87	22	67	2·4	0·4–13·2	0·3
Consumed sheep (mutton or lamb)	5	33	15	47	0·3	0·03–2·6	0·3
Where meat was consumed							
At home	12	67	21	75	0·3	0·03–3·2	0·3

Table 3 (*cont.*)

Risk factor	Cases *n*	Cases %	Controls *n*	Controls %	OR*†	95% CI	*P* value
At restaurant	4	25	9	32	0·9	0·2–4·6	0·9
How meat was prepared							
Pink in middle	5	8	5	4	2·7	0·5–15·0	0·2
Boiled	48	76	84	67	1·8	0·8–4·0	0·2
Grilled	9	15	12	10	1·3	0·4–3·8	0·6
Roasted	17	28	46	38	0·6	0·3–1·2	0·1
Kinkali (dumplings)	29	47	69	54	0·7	0·4–1·5	0·4
Shashlik (grilled barbecue)	23	36	58	46	0·6	0·3–1·3	0·2
Would eat meat from sick livestock	59	92	113	88	2·0	0·6–7·3	0·3
Would eat meat from livestock found dead	60	95	112	88	5·0	1·0–24·8	0·05
Travel‖	13	20	17	13	1·7	0·7–4·1	0·3
Handled livestock products	33	51	27	22	**4·0**	**1·9–8·4**	**<0·001**
Bones/horn	9	41	4	18	1·4	0·08–23·6	0·8
Skin/hide	16	62	4	17	3·0	0·3–28·8	0·3
Leather	12	55	7	30	2·6	0·3–25·2	0·4
Insect bite	53	88	127	97	**0·2**	**0·03–0·8**	**0·02**
Work with soil							
Near sick or dead livestock	61	97	118	95	1·6	0·2–10·1	0·6
Near livestock burial site	15	94	36	95	0·7	0·04–11·8	0·8
Near other earthworks	42	65	75	58	1·5	0·6–3·4	0·4
While gardening	9	64	27	59	0·6	0·1–4·2	0·6
Covered injury while working soil	2	11	13	34	0·2	0·02–2·0	0·2
Total	67	100	134	100	–	–	–

OR, Odds ratio; CI, confidence interval.
* All values shown in bold indicate a significant difference ($P < 0·05$).
† All ORs and corresponding 95% CIs are calculated comparing cases to controls.
‡ Livestock-related occupations included herder/shepherd, farmer/rancher, livestock worker, and veterinarian.
§ Cleaning defined as removing animal waste and/or dirty bedding.
‖ Participant travelled outside place of residence/village.

Table 4. *Participants' responses to animal management questions, 2012 anthrax cross-sectional assessment in Georgia (n = 131)*

Variable	Yes *n*	Yes %	No *n*	No %
Livestock anthrax vaccination	53	44	68	56
Did not know about vaccine	10	67	5	33
Unable to afford vaccine	12	75	4	25
Move livestock >1 km	19	16	97	84
Had sick livestock	15	12	110	88
Sick livestock had anthrax symptoms	9	64	5	36
Sick livestock died	8	80	2	20
Sell or slaughtered sick livestock for consumption	2	20	8	80
Had livestock die suddenly	11	9	117	91
Processed for consumption	2	25	6	75

subsequent animal deaths; two of 10 reported sick animals were sold or slaughtered for consumption. Sudden death in animals was also reported, some of which were processed for meat.

DISCUSSION

Descriptive epidemiology and control strategies.

According to the GIDEON database [13], human cutaneous anthrax in Georgia increased after funding for control programmes began to decline in 1989. In 2007, responsibility for providing livestock anthrax vaccinations shifted to individual farmers which probably led to a decrease in vaccinations administered and a resulting increase in livestock cases. The bimodal peaks in the 2012 anthrax outbreak of both livestock and human cases were unusual. The June peak was preceded by heavy rainfall in May, which was three times greater than the rainfall observed in June, which itself was 1·5 times less than the previous 30-year average. Additionally, the October peak in Kvemo Kartli occurred after July where rainfall was twofold higher and August rainfall was twofold less than the previous 30-year average. No significant changes in average temperatures were recorded by the Georgia National Environmental Agency. This pattern of outbreak peaks occurring in dry or normal precipitation months following months where heavy rains occurred has been reported elsewhere for previous livestock anthrax outbreaks [14, 15]. Two suggested mechanisms include: (1) new grass growth and loosened soil, due to rain, increasing the likelihood of spore ingestion by livestock on contaminated pastures and (2) emergence of excess biting flies implicated in mechanical transmission [16]. Further investigation of the ecological relationships in Georgia between weather patterns and outbreaks of anthrax is warranted.

The significant increase in human anthrax cases in 2012 indicated an even larger outbreak exceeding the already increasing trend in cases. The high proportion of human cases in Kvemo Kartli and Kakheti could be related to those regions containing 40% of Georgia's susceptible livestock. However, a parallel increase in livestock anthrax was not identified, in part because livestock deaths are often not reported. Additionally, human cases were not commonly linked to specific livestock case exposures, due partially to a lack of coordinated anthrax case investigation between medical and veterinary authorities. Only two of the human cases investigated in this outbreak were linked to the same exposure source, the slaughter of an infected sheep; otherwise, households or clusters of households with more than one case were not noted.

Interestingly, no gastrointestinal cases were reported in this outbreak. Mild cases with non-specific gastroenteritis symptoms either may not seek medical care or anthrax may not be suspected [2]. Moreover, hyperacute cases may avoid diagnosis as they die before receiving medical attention [2]. Additionally, there is a high background level of diarrhoeal disease in Georgia including hemorrhagic diarrhoea [17], which could reduce the index of suspicion for anthrax as an aetiological cause. There are also existing cultural preferences in Georgia against consuming raw or under-cooked meat, which may limit the occurrence of gastrointestinal anthrax.

Case-control investigation

Most human anthrax outbreaks are generally related to livestock anthrax cases or outbreaks [5, 6]. In this investigation, all risk factors significantly associated with disease were related to exposure to livestock or their products. After multivariable analysis, dead livestock disposal and animal slaughter were the independent predictors most strongly associated with disease; this was especially true for those slaughtering their own livestock. Slaughtering sick livestock has been reported in other countries as a routine practice in an attempt to recover some of their investment [18]; this investigation provides evidence that meat from sick livestock and livestock found dead was processed for sale or consumption, probably to minimize economic loss. There is no policy in Georgia for compensation of livestock losses, which may prompt residents to resort to this activity. In addition, persons may not be aware of the risks of anthrax associated with butchering, handling, or consuming meat from infected animals [18]; in this investigation, most cases (92%) and controls (88%) reported that they would consume livestock that were found to be sick, or dead (95% and 88%, respectively).

The strongest association found among individual potential risk factors was caring for sick livestock. Contact with sick or dying anthrax-infected livestock has previously been demonstrated to be the principal source of human agricultural exposures [2, 5, 6]. Cutaneous anthrax can occur when agricultural and veterinary workers handle, slaughter, perform necropsy on, or dispose of affected and dead animals [19]. Those who owned livestock, especially cattle and goats, had higher odds of becoming infected than controls. Dog ownership and horse ownership were also significantly associated. However, this is probably the result of close correlation between dog and horse ownership and cattle ownership, as 91% and 92% of dog and horse owners, respectively, also owned cattle. Horse meat is not commonly consumed in Georgia, limiting human exposures to equine carcasses. Furthermore, equine anthrax has been reported rarely in Georgia, and without any associated human cases reported. Canines are considered relatively resistant to infection [3, 20], and no canine cases have been reported in the OIE WAHID database [11].

Another strong association was seen with those who handled livestock products such as meat, skin, leather, or bones. No specific livestock species or product type was found to have higher odds for infection; however, handling and bringing meat from diseased animals into the household was found to be associated with disease in an investigation of anthrax in Haiti [21].

In our investigation, eating meat from one's own farm was a risk, as was slaughtering one's own livestock and slaughtering livestock that were found sick; however, buying meat from a butcher's shop was protective. It is likely that human anthrax exposures and cases occurred when people slaughtered and butchered their own potentially infected animals, whereas regulations requiring meat sold in markets and butcher's shops to originate from inspected slaughterhouses potentially reduced the risk of meat from infected animals being sold there.

As expected, those who worked in livestock-related occupations were at higher risk of developing anthrax; however, no single occupation classification was significantly associated. Both herding and cleaning animal waste or dirty bedding were identified as higher-risk farm activities. Each involves working closely with livestock or their environment. Agricultural field work was not associated with disease in this investigation; however, it was previously identified as a self-reported source of exposure in Georgia [22]. It was noted that this exposure source is not well documented and the reports may result from recall bias or an unwillingness to disclose slaughtering of infected animals [22].

Three species of blood-feeding insects were able to mechanically transmit anthrax to guinea pigs and mice in one study [4]; however, we found bites from blood-feeding insects were more frequently reported by controls compared to cases. We did not determine the species of biting insects; therefore, different species may have been involved with controls and cases based on their locations relative to animal carcasses, which may explain this finding. Additionally, biting flies are more frequently associated with livestock outbreaks than with human cases since they only occasionally bite humans [16].

We found slaughter and disposing of dead animals to remain strong independent predictors of human disease in multivariable analysis. We also emphasize the univariate analysis results demonstrating that increased risk is primarily related generally to occupational contact with livestock and meat for consumption due to the level of multicollinearity between individual characteristics and behaviours elicited in the questionnaire.

Cross-sectional assessment

Most cross-sectional assessment participants did not vaccinate their livestock. Given the cessation of national anthrax vaccination campaigns in Georgia in 2007 and subsequent decrease in anthrax vaccine administration, reinstitution of annual government-sponsored vaccination programmes may be necessary, particularly in endemic regions. Livestock vaccination remains a mainstay of control, reducing animal disease incidence, sometimes to the point of elimination, thereby reducing human exposures to infected livestock and animal products and consequent illness [10, 23].

Only a few respondents reported moving livestock >1 km from where they were pastured on the day of interview; however, both free-roaming and shepherded livestock were observed within and near many communities. This question was important to determine any role of animal movement in exposure, such as exposing animals to areas containing anthrax carcass burial sites. Regardless, livestock anthrax appeared to be localized and not resulting from exposures in other regions, such as may arise in animals migrating from pastures in other regions of the country.

The cross-sectional assessment explored health outcomes in livestock, with two-thirds of respondents reporting acute illness and/or head or neck swelling, clinical signs associated with anthrax infections. These findings suggest there were livestock anthrax cases not being identified and reported. After finding dead livestock, approximately one-fifth of respondents processed the carcasses for human consumption; again this salvage practice most likely occurred to minimize economic loss, but potentially resulted in human exposures and illness. Public health and animal health messaging can help inform livestock owners to recognize anthrax, of the value of veterinary examinations, and of the human health risks from slaughtering and consuming sick livestock or carcasses. The introduction of compensation for livestock losses that are properly notified to authorities, with subsequent investigation, response and appropriate decontamination may help reduce the occurrence of salvage slaughter and butchering of anthrax-infected animals. Alternatively, the introduction of insurance for livestock, whereby compensation is provided if anthrax occurs in animals that are appropriately vaccinated, can help promote vaccination as a preventive practice and mitigate economic loss, thus reducing the likelihood that anthrax-affected meat will enter the food chain.

Limitations

Survey participants were similar demographically except for specific occupations related to livestock. Since controls were those who were at home at the time of the interview visit, control participants were possibly biased towards those who did not participate in fieldwork or have livestock-associated occupations, which could increase the value of the odds ratio. Our results were also potentially influenced by differential recall bias and false reporting. Persons without anthrax may not remember exposure history during the time period of risk for the matched cases. This may lead to differential under-reporting of exposure by controls, and increase the value of the odds ratio. By contrast, cases may not admit their participation in slaughter of sick livestock or sale of meat from a sick animal; this was identified by NCDC investigators as a practice with origins during the Soviet period, when such activities would result in punitive measures from the government [24, 25]. This under-reporting of exposure by cases could lower the value of the odds ratio.

Other limitations were related to the questions regarding livestock anthrax vaccination. The timing of vaccination relative to the occurrence of anthrax in any animal in the interviewee's or a neighbouring herd was not ascertained by the questionnaire, so we were unable to assess a temporal relationship between livestock vaccination and either human or animal anthrax cases. It was therefore possible that a respondent would report that they had vaccinated their livestock for anthrax, but only after the disease had appeared in either their herd or a neighbouring herd; one case reported vaccinating his animals only after he had developed anthrax himself.

We were unable to obtain responses to follow-up questions related to knowledge of anthrax prevention practices in livestock and the ability to afford vaccinations from over three-quarters of participants who did not vaccinate, so these results should be interpreted with caution. These topics may potentially be sensitive resulting in participants' reluctance to respond or to provide factual responses. Regardless, we think that both vaccine knowledge and affordability are important factors to explore with regard to intervention recommendations.

Recommendations

It was evident that handling carcasses, sick livestock, or associated livestock products were significant risk factors for human disease; people should be discouraged from handling possible anthrax-infected livestock or products in any form, unless properly trained and wearing appropriate personal protective equipment. The combination of compensation programmes to prevent the slaughter and sale of meat from infected animals and nationally sponsored anthrax vaccination campaigns in livestock may reduce the burden of human and animal disease; such programmes could be initially focused in areas with recent reports of animal or human cases. The NFA started prophylactic anthrax vaccination of cattle in the predominantly affected regions of Kvemo Kartli and Kakheti at the end of 2012 and in 2013. Finally, we encourage collaboration between relevant partners to develop and distribute health messaging on control and recognition of anthrax in humans and animals, integration of disease surveillance, and collaborative investigation of anthrax cases. According to the ProMED database [26], such an investigation occurred in August 2013, where a joint human and animal health investigation of a human anthrax case in Tbilisi, Georgia identified the exposure source as meat sold in a market, ultimately traced back to an illegal, uninspected source. The response included decontamination and cessation of further sale of suspect meat at the market, with no subsequent human cases reported.

APPENDIX. The anthrax investigation team

Z. Asanishvili[1], T. Napetvaridze[1], S. Guramishvili[2], M. Lashkarashvili[2], N. Mamuchishvili[2], S. Huseynova[3], M. Shikhiyev[3], M. Abdullayev[3], E. Zeynalov[3]

[1] *Georgia National Food Agency, Georgia Ministry of Agriculture, Tbilisi, Georgia*

[2] *Georgia National Center for Disease Control and Public Health, Georgia Ministry of Health, Tbilisi, Georgia*

[3] *South Caucasus Field Epidemiology and Laboratory Training Program, Tbilisi, Georgia*

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DECLARATION OF INTEREST

None.

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