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Impact of traditional cutaneous scarification on anthrax lesions: A series of cases from Cubal, Angola

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ABSTRACT

Objectives: *Bacillus anthracis* infection is a worldwide zoonosis that affects the most vulnerable population and has a high mortality rate without treatment, especially in non-cutaneous presentations. Cutaneous scarification is still common in some regions of the world for the treatment of certain diseases as part of traditional medicine. We describe a series of cutaneus anthrax from a rural setting in Angola where cutaneus scarification is common.

Case presentation: This is a retrospective observational study describing a series of cutaneous anthrax cases from Cubal (Angola), many of whom were treated with skin scarification before admission. A total of 26 cases were diagnosed from January 2010 to December 2018. None of the cases were confirmed and eight (30.8%) were probable cases according to the Centers for the Disease Control and Prevention anthrax case definition. The median age was 11 (4.7-30.5) years, 17 (65.4%) had lesions on the head, face, or neck and 15 (57.7%) were treated with cutaneous scarification. Nine (34.6%) patients died. Traditional cutaneous scarification was significantly associated with cutaneous superinfection, respiratory, systemic involvement, and death.

Conclusion: Our case series points to increased complications and worse outcome of cutaneous anthrax disease if treated with skin scarification.

Introduction

Anthrax is a worldwide zoonosis caused by *Bacillus anthracis*, a Gram-positive spore-forming bacterium. Many animals are susceptible, although grazing herbivores are the most commonly affected and the usual source of infection for humans. Herbivores often become infected by *B. anthracis* spores from the soil when grazing and then return the spores to the soil when they die. The spores can last in the soil for decades, depending mainly on climatic conditions and soil composition [1].

In humans, infection usually occurs through skin lesions after direct contact with infected animals or animal products such as carcasses or hides. Less frequently, transmission can occur through the ingestion of contaminated meat or water, inhalation of spores presents in animal products such as wool [2], or through an intentional release of spores [3]. In recent years, there has been growing concern following the description of an unrecognized form of transmission found in parenteral drug users (injectional anthrax) [4]. In non-endemic countries, the infection is mostly considered an occupational disease. On the contrary, in endemic regions such as the Sub-Saharan Africa, many people are at risk given the favorable climatic conditions for the outbreaks, the lack or insufficient livestock vaccination, and the close contact of livestock with a large part of the population [1].

The disease has three main forms of presentation: cutaneous, respiratory, and gastrointestinal. In some cases, lymphohematogenous spread can lead to central nervous involvement and sepsis. Cutaneous anthrax is the most frequent presentation and occurs after infection of a wound or skin abrasion. The usual presentation is a small papule that is surrounded by vesicles in the first 48 hours and evolves into a painless black eschar with edema that

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may resolve in weeks [5]. With proper treatment, the case fatality rate of cutaneous anthrax is expected to be less than 1%. However, death due to systemic involvement can occur in a 10-40% of untreated cases [6]. Gastrointestinal, inhalation anthrax, septicemia, and meningitis have a high mortality because of the low index of suspicion, later diagnosis, and delayed initiation of treatment [7]. Treatment of *B. anthracis* infection depends on the form of presentation and the severity of the disease. B-lactams as penicillin, amoxicillin or carbapenems, linezolid, fluroquinolones, and tetracyclines are the mainstay of treatment and a combination of antibiotics is recommended for non-cutaneous forms. Moreover, antitoxins such as raxibacumab, obiltoxaximab, or anthrax immune globulin should be added to the treatment in systemic and severe forms [8]. Finally, and although surgery is not usually indicated in cutaneous anthrax, debridement may be necessary in severe cutaneous cases, especially in those lesions related to heroin skin poppers [9].

Traditional healers are widespread in most Sub-Saharan African countries and a large part of the population, especially in rural areas, believes in and adheres to the therapies offered by these practitioners. Cutaneous scarification, which consists of applying superficial cuts, lacerations, burns, or other types of wounds to the skin, is one of the therapies they perform. Although the purposes of this practice are multiple (aesthetic motives, symbols of cultural identity, or rituals of passage from childhood to adulthood), in Angola, it is commonly used to treat states of illness [10]. The usual skin scarification treatment involves the performance of shallow cuts on the skin and the application of local herbs to the wounds. Clinical events such as convulsions or ascites are known to be treated by skin scarification [11]. To date, the benefits of these practices have not been demonstrated. On the contrary, various diseases such as dermal hypertrophy, tetanus, bacterial superinfection, and transmission of infections such as hepatitis C virus and HIV can occur [12].

The aim of this study was to describe a case series of cutaneous anthrax cases diagnosed at Hospital Nossa Senhora da Paz (Cubal, Angola) and assess the impact that the skin scarification of the lesions practiced by traditional healers had on the evolution of the patients.

Methods

This is an observational retrospective study, where medical records of patients with a diagnosis of cutaneous anthrax registered at the Nossa Senhora da Paz Hospital (Cubal, Angola) from January 2010 to December 2018 were reviewed. Cubal is a municipality of the province of Benguela (Angola), with a population of 320,000 inhabitants. It is located in the highlands of the central plateau of Angola, and it is divided into four communes. Cubal has two referral hospitals, the Hospital Municipal (HM), a 177-bed public hospital located in the center of Cubal Sede (main commune), and the Hospital Nossa Senhora da Paz (HNSP), a non-profit 300-bed private institution integrated into the public health system located on the outskirts of Cubal Sede.

The inclusion criteria were patients presenting characteristic cutaneous lesions of anthrax disease and classification was done according to the Centers for the Disease Control and Prevention (CDC) anthrax case definition [13]. According to this case definition, a suspected case was defined as a case that met the clinical criteria and for whom an anthrax test was ordered but with no epidemiologic evidence relating it to anthrax. A probable case was defined as a case that met the clinical criteria and had presumptive laboratory test results or a case that met the clinical criteria and had epidemiologic evidence relating it to anthrax. A confirmed case was defined as a case that met the clinical criteria and had confirmatory laboratory test results.

Epidemiological and clinical characteristics from included patients were collected: demographic information (age, sex, commune of residence, and suspected source of infection), clinical information; number and location of lesions, cutaneous superinfection (impetigo, cellulitis, and abscesses), perilesional edema, fever, neurological involvement (altered mental status measured through Glasgow Coma Scale, headache, and meningeal signs), respiratory involvement (respiratory distress, thoracic pain and cough), gastrointestinal involvement (nausea, vomiting, and abdominal pain), and systemic involvement (including fever, neurological, respiratory, and gastrointestinal involvement) defined as per the CDC [13], performance and result of gram staining, treatment received (traditional skin scarification and antibiotic therapy), and the final outcome.

Data management

The database was designed in Microsoft Excel, and it was transferred to the SPSS software for Windows (Version 19.0; SPSS Inc, Chicago, IL, USA) for the statistical analysis. Qualitative variables were expressed as absolute numbers and percentages, whereas quantitative ones were expressed through means and SDs or median and interquartile range, depending on the distribution. The χ^2 test or Fisher's exact test, when appropriate, was used to compare the distribution of categorical variables, and the Student's *t*-test was used for continuous variables. The results were considered statistically significant if the two-tailed *P*-value was <0.05.

Ethical disclosure

Procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki as revised in 2013. The protocol for this study was approved by the ethics committee of the Ministry of Health of Angola (n°30/C.E.M.S/2023). Written informed consent was not obtained because of the retrospective nature of the study, although oral consent was obtained from all subjects or their guardians for the taking of the photographs.

Results

Sociodemographic characteristics

A total of 26 persons were diagnosed with cutaneous anthrax during this period. According to the CDC anthrax case definition, none of the cases were confirmed, eight (30.8%) were classified as probable anthrax, and the rest were suspected cases. The median age was 11 (4.7-30.5) years, 18 (69.2%) individuals were $\leq$15 years old, and 17 (65.4%) were men. A total of 23 (96.2%) patients were from Cubal municipality. A total of 20 (76.9%) patients were diagnosed during the rainy season (October to April) and 17 (85%) of them during the months of October to December. Only two (7.7%) patients reported occupational exposure (cattle) and four (15.4%) reported history of contact or ingestion of spoiled meat and one of them clearly reported consuming meat from an animal suspected of hemorrhagic anthrax death (Table 1).

Clinical findings

A total of 18 (69.2%) patients presented perilesional edema surrounding the skin lesion. The median number of days from the onset of skin lesions to hospital consultation was 4 (3-6.25) days. Six (23.1%) patients had two cutaneous lesions, whereas the rest presented only one. A total of 17 (65.4%) patients presented skin lesions in the head, face, or neck; three (11.5%) in the upper limbs; and two (7.7%) in the thorax (Figure 1). A total of 15 (57.7%) patients reported having traditional treatment consisting in scarifications of the cutaneous lesions. A total of 13 (86.6%) of those

Table 1
Description of cutaneous anthrax cases.

Patient	Age[a]	Diagnosis date	Sex	Site of lesion	Source of exposure	Skin lesion scarification	Skin Superinfection	Perilesional edema	Fever	Neurologic involvement	Respiratory involvement	Gastrointestinal involvement	Gram stain (sample)	Treatment	Outcome
1	63	11/2010	Male	Jaw	Shepherd	Yes	Present	Absent	Absent	Absent	Present	Absent	Positive (skin lesion)	-	Death> 48 hours
2	41	11/2010	Male	Thorax	Shepherd	Yes	Present	Present	Absent	Present	Absent	Absent	Positive (skin lesion)	-	Death> 48 hours
3	14	07/2012	Male	-	-	No	Absent	Absent	Absent	Absent	Absent	Absent	-	-	Recovered
4	5	02/2013	Male	Jaw	-	Yes	Present	Present	Present	Present	Present	Present	-	Ampicillin	Death> 48 hours
5	41	07/2013	Female	Neck	-	Yes	Present	Present	Present	Absent	Present	Present	-	Penicillin	Recovered
6	1	10/2013	Male	Upper limb	-	Yes	Present	Present	Present	Absent	Absent	Absent	-	Amoxicillin-clavulanate	Recovered
7	1	10/2013	Male	Front	-	Yes	Present	Present	Present	Absent	Absent	Absent	-	Ampicillin	Recovered
8	41	10/2013	Female	Face and nose	-	Yes	Present	Present	Absent	Absent	Present	Present	-	-	Death> 48 hours
9	3	11/2013	Female	Face	-	No	Absent	Present	Present	Present	Absent	Present	-	Ampicillin	Recovered
10	5	11/2013	Male	Face	-	No	Absent	Present	Present	Absent	Absent	Absent	-	Ampicillin	Recovered
11	12	11/2013	Female	Jaw	-	No	Absent	Present	Absent	Absent	Absent	Absent	-	Ampicillin	Recovered
12	7	11/2013	Male	Eyelid and forehead	-	No	Absent	Present	Present	Present	Absent	Absent	-	Ampicillin	Recovered
13	0.75	01/2014	Male	-	-	No	Absent	Absent	Absent	Absent	Absent	Absent	-	-	Voluntary discharge
14	9	07/2014	Male	Eyelid and Jaw	-	No	Absent	Absent	Present	Absent	Present	Absent	-	Amoxicillin-clavulanate	Recovered
15	15	08/2014	Male	Head and neck	-	No	Absent	Present	Absent	Absent	Absent	Absent	-	Ampicillin	Voluntary discharge
16	12	10/2014	Female	-	Ingestion of spoiled meat	No	Absent	Present	Present	Absent	Absent	Absent	-	Ampicillin	Recovered
17	9	10/2014	Male	-	Ingestion of spoiled meat	No	Absent	Absent	Present	Absent	Absent	Absent	-	Ampicillin	Recovered
18	48	12/2014	Female	Face and upper limb	-	Yes	Absent	Absent	Absent	Present	Absent	Absent	Positive (cere-brospinal fluid)	-	Death<48 hours
19	42	12/2014	Female	-	-	No	Absent	Absent	Absent	Absent	Absent	Absent	-	-	Recovered
20	10	12/2014	Female	Eyelid	-	Yes	Present	Present	Present	Present	Absent	Absent	-	Penicillin + ciprofloxacin	Recovered
21	3	11/2015	Male	Face and Eyelid	-	Yes	Present	Present	Absent	Present	Present	Absent	-	Ceftriaxone	Death< 48 hours
22	4	11/2015	Male	Thorax	-	Yes	Present	Present	Present	Absent	Absent	Present	-	Ceftriaxone	Death< 48 hours
23	5	12/2015	Male	Head	-	Yes	Present	Present	Present	Absent	Absent	Absent	Positive (skin lesion)	Penicillin + gentamicin	Recovered
24	20	03/2017	Male	Hand	Ingestion of spoiled meat	Yes	Absent	Absent	Present	Absent	Present	Present	-	Penicillin + ciprofloxacin	Voluntary discharge
25	27	06/2017	Female	Eyelid	-	Yes	Present	Present	Present	Present	Present	Absent	-	Penicillin + ciprofloxacin	Death> 48 hours
26	12	05/2018	Male	Jaw	Ingestion of spoiled meat	Yes	Present	Present	Present	Present	Present	Present	-	Ceftriaxone	Death < 48 hours

[a] Age (years).(-) no information available.

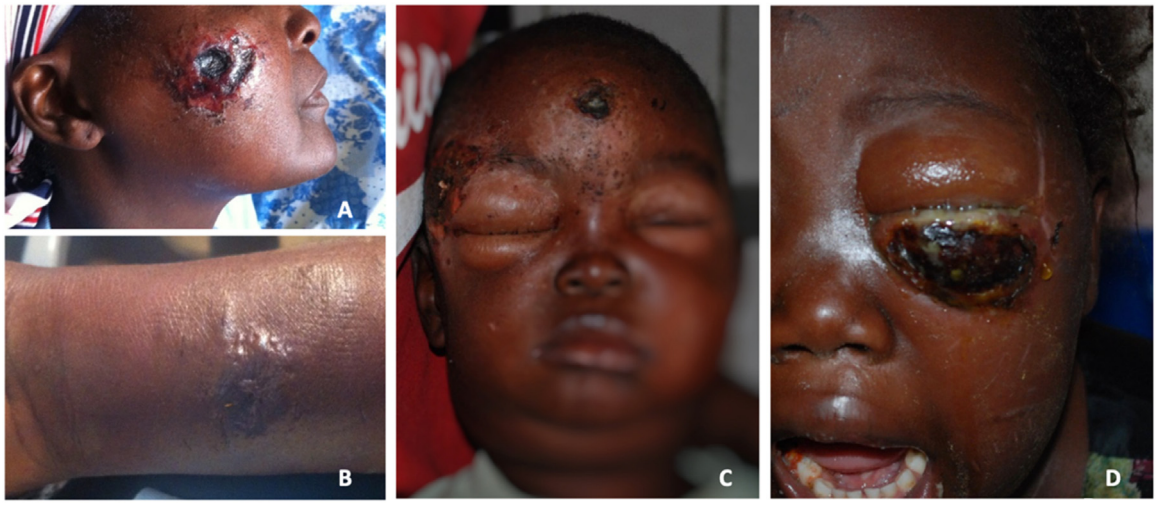

Figure 1. Cutaneous anthrax lesions. Images A and B show the lesions on the face and upper limb with signs of cutaneous scarification of case n° 18. Image C shows the lesions on the forehead and eyelid with associated edema of case n° 12. Image D shows the lesion on the eyelid with signs of superinfection of case n° 20.

presented signs of cutaneous superinfection, nine (60%) of them with signs of cellulitis and/or impetigo, and five (33.3%) with cutaneous abscesses. No cutaneous superinfection was observed in those who had not received skin scarification ($P = 0.008$). Fever was present in 16 (61.5%) patients. Nine (34.6%) had neurological symptoms: six were obnubilated and three with coma (Glasgow Coma Scale <8), four reported headache, and one presented meningeal signs and hemiparesis. Nine (34.6%) patients presented respiratory symptoms, four of them had respiratory distress, four had chest pain, and two reported cough. Finally, four (15.4%) patients had gastrointestinal symptoms consisting of abdominal pain in two cases and nausea and vomiting in the remaining two. Finally, 21 (80.8%) patients presented systemic involvement.

Diagnosis and treatment

The presence of short-chain, square-ended, Gram-positive bacilli compatible with *B. anthracis* was demonstrated in only four (15.4%) cases. Three samples were taken from the skin lesions and one in a cerebrospinal fluid sample. Treatment information was available in 19 (73.1%) patients. A total of 15 (78.9%) received betalactams, three (15.8%) received betalactams plus quinolones, and one (5.3%) received betalactams plus aminoglycosides.

Outcome

Nine (34.6%) patients died, four (44.4%) of them within the first 48 hours of hospitalization, fourteen (53.9%) recovered, and three (11.5%) were voluntarily discharged. All patients who died presented systemic involvement and had been treated with skin scarification, which was significantly associated with an unfavorable outcome (death) ($P = 0.007$) (Table 2). Moreover, traditional treatment through scarification of the skin lesions was significantly related to the presence of cutaneous superinfection, respiratory symptoms, and systemic involvement as seen in Table 3.

Table 2
Sociodemographic and clinical variables and its relation to an unfavorable outcome.

	Death	*P*-value
Sex (men)	6/15 (40%)	0.74
Age (≤ 15 years)	4/18 (22.2%)	0.078
Localization of the lesion (head/neck)	6/15 (40%)	0.43
Number of lesions (≥ 2)	3/6 (50%)	0.6
Perilesional edema	5/13	0.3
Skin scarification	9/15 (60%)	0.007
Systemic involvement	9/21(42.8%)	0.12

Discussion

This case report series of cutaneous anthrax from Cubal (Angola) has shown a male and young age predominance, a higher mortality compared with other reports, and a worse prognosis in those patients who were treated with skin scarification as part of regional traditional medicine.

A total of 15 (57.7%) patients received skin scarification before admission to HNSP, which demonstrates the high degree of adherence to this practice in the area. All but two of those who received this traditional therapy presented signs of cutaneous superinfection, whereas no superinfection was seen in those who did not receive it. Regarding the final outcome, nine (34.6%) patients died, almost half of them within the first 48 hours of admission. All of them presented systemic involvement. Our series of cases has shown a greater mortality compared with other reports in the literature [14,15]. In this sense, we have observed that patients who received skin scarification before admission had significantly more cutaneous superinfection and respiratory and systemic involvement, as well as an unfavorable outcome (death). Although bacteriemia related to cutaneous superinfection could be wholly or partially responsible for a worse prognosis, scarification of anthrax lesions probably played a role in the spread of the disease. In fact, it has been stated that surgery for cutaneous anthrax should be avoided because of the risk of dissemination and poorer outcomes, especially in the vesicular phase of the lesion [16,17]. Moreover, our results are in line with those of a retrospective review of cutaneous anthrax in which skin trauma was significantly associated with an increased risk of death [7].

Pediatric cases of anthrax are usually less frequent than those in adults, probably because of a lower risk of exposure to *B. anthracis* spores [18,19]. As an explanation for our findings, we believe it is likely that in this area, there is greater peridomestic contact with livestock or intradomestic contact with livestock products. In addition, it is common for young children to accompany family members to work (slaughterhouse, informal markets, and fields), where they may also come into contact with spores from the soil, from the livestock, or animal products. Interestingly, 65.4%

Table 3
Skin scarification and its relation to clinical findings and outcome.

	Skin scarification (n = 15)	No skin scarification (n = 11)	*P*-value
Cutaneous superinfection	13 (86.6%)	0 (0.0%)	$P = 0.008$
Neurologic symptoms	7 (46.6%)	2 (18.2%)	$P = 0.217$
Respiratory symptoms	8 (53.3%)	1 (9.1%)	$P = 0.036$
Gastrointestinal symptoms	3 (20.0%)	1 (9.1%)	$P = 0.614$
Systemic involvement	15 (100.0%)	6 (54.5%)	$P = 0.007$
Outcome (death)	9 (60.0%)	0 (0.0%)	$P = 0.007$

Values are expressed as number and percentage otherwise specified.

of patients had skin lesions on the face, head, or neck; however, no association with worse prognosis was found.

In relation to the diagnosis, none of the cases included in our series had a confirmed diagnosis because the only diagnostic test available was microscopy. Although the microscopic characteristics of *B. anthracis* are quite specific, the description of Gram-positive rods, square-ended, in pairs or short chains, does not allow differentiating *B. anthracis* from *Bacillus cereus* biovar *anthracis* [20]; therefore, ideally, all cases of suspected anthrax should be confirmed by culture and identification or other techniques such as polymerase chain reaction [13].

Regarding antibiotic therapy, the most used antibiotics were B-lactams and four patients received dual therapy. Ampicillin is no longer recommended for the treatment of anthrax because of the high percentage of resistant isolates described; despite that, regional or local resistant profiles might differ [21,22]. In our sample, nine patients were treated with ampicillin, and all but one survived. Ceftriaxone, which should not be considered for anthrax disease nor for cutaneous superinfection, was given to three patients who died within the first 48 hours of admission. Wild-type strains of *B. anthracis* have constitutive inducible B-lactamases that can hydrolyze cephalosporines [22,23]. Ceftriaxone was probably used as a desperate treatment given the severity of the cases (two of them were in coma at the time of admission) and to empirically treat other possible etiologies that commonly cause central nervous system infections. In addition, the lack of stock of other intravenous antibiotics and the lack of initial clinical suspicion of anthrax could have played a role in administering this antibiotic.

Finally, and as previously commented, dual and triple therapy is usually recommended for non-cutaneous and severe cases. In our series, only four (19.1%) of the 21 patients who presented systemic involvement received dual therapy and none received triple therapy. Three patients received B-lactams plus quinolones and only one recovered from the disease. The remaining patient, who presented extensive edema and fever, received dual therapy with B-lactams and aminoglycosides and recovered from the disease. Although aminoglycosides are not considered for anthrax treatment, reports from a large cohort from France has described a 100% sensibility to gentamicin and streptomycin [24]. In addition, some studies have found that aminoglycosides have activity against anthrax lethal factor (virulence factor), which could provide an added value [25,26].

Our study has several limitations; on the one hand, it has a retrospective nature. Data were not collected systematically; thus, there is missing information in some cases. However, we have been able to collect the most relevant and interesting information for the purpose of our study, which was the relationship between skin scarification and prognosis. On the other hand, most cases were possible or probable cases, with none of the cases with microbiological confirmation because of the limitations of the laboratory of HNSP. In any case, most of the published cohorts of anthrax cases are based on clinical suspicion, and the epidemiology and the skin lesions make it very likely that all the reported cases are truly cutaneous anthrax. Sampling for microbiological confirmation was low. This may be related to various conditions, such as the cost of complementary tests that have to be paid by patients, the lack of initial clinical suspicion, and the lack of knowledge about the diagnosis of the disease.

In conclusion, most cases of cutaneous anthrax were seen in children or young males, and more than half were treated with pre-admission skin scarification. Antibiotic treatment was difficult because of limited options and the lack of initial clinical suspicion. Mortality was high and was related to the practice of traditional skin scarification. Policies should be adopted to raise awareness among the community and the healers about the risks of this practice to control and limit it.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethics approval and consent to participate

Procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki as revised in 2013. The protocol for this study was approved by the ethics committee of the ministry of health of Angola (n°30/C.E.M.S/2023). Written informed consent was not obtained due to the retrospective nature of the study.

Author contributions

JMC: conceptualization, data management, writing original draft; MM conceptualization, data collection, writing original draft; FS: methodology, data analysis, review & editing; EBT: review & editing; AN: data collection; MLA: conceptualization, supervision, review & editing; and IM: supervision, review & editing.

Consent for publication

Oral consent was obtained from all subjects or their guardians for the taking of the photographs.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Author information

Dr. Joan Martínez-Campreciós is an internal medicine physician and researcher at Vall Hebron Hospital, Barcelona, Spain. His research interests are tuberculosis, neglected tropical diseases, and viral hepatitis.

References

[1] Carlson CJ, Kracalik IT, Ross N, Alexander KA, Hugh-Jones ME, Fegan M, et al. The global distribution of *Bacillus anthracis* and associated anthrax risk to humans, livestock and wildlife. *Nat Microbiol* 2019;**4**:1337–43. doi:10.1038/s41564-019-0435-4.

[2] Spencer RC. Bacillus anthracis. *J Clin Pathol* 2003;**56**:182–7. doi:10.1136/jcp.56.3.182.

[3] Jernigan JA, Stephens DS, Ashford DA, Omenaca C, Topiel MS, Galbraith M, et al. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. *Emerg Infect Dis* 2001;**7**:933–44. doi:10.3201/eid0706.010604.

[4] Ascough S, Altmann DM. Anthrax in injecting drug users: the need for increased vigilance in the clinic. *Expert Rev Anti Infect Ther* 2015;**13**:681–4. doi:10.1586/14787210.2015.1032255.

[5] Swartz MN. Recognition and management of anthrax–an update. *N Engl J Med* 2001;**345**:1621–6. doi:10.1056/NEJMra012892.

[6] Doganay M, Metan G, Alp E. A review of cutaneous anthrax and its outcome. *J Infect Public Health* 2010;**3**:98–105. doi:10.1016/j.jiph.2010.07.004.

[7] Thompson JM, Cook R, Person MK, Negrón ME, Traxler RM, Bower WA, et al. Risk factors for death or meningitis in adults hospitalized for cutaneous anthrax, 1950–2018: a systematic review. *Clin Infect Dis* 2022;**75**:S459–67. doi:10.1093/cid/ciac533.

[8] Hesse EM, Godfred-Cato S, Bower WA. Antitoxin use in the prevention and treatment of anthrax disease: a systematic review. *Clin Infect Dis* 2022;**75**:S432–40. doi:10.1093/cid/ciac532.

[9] Ringertz SH, Høiby EA, Jensenius M, Maehlen J, Caugant DA, Myklebust A, et al. Injectional anthrax in a heroin skin-popper. *Lancet* 2000;**356**:1574–5. doi:10.1016/S0140-6736(00)03133-0.

[10] Garve R, Garve M, Türp JC, Fobil JN, Meyer CG. Scarification in sub-Saharan Africa: social skin, remedy and medical import. *Trop Med Int Health* 2017;**22**:708–15. doi:10.1111/tmi.12878.

[11] Tsiba JB, Mabiala-Babela JR, Lenga LI, Likiby D, Bounkouta AC, Moussodji D, et al. Scarifications chez l'enfant hospitalisé au Congo [Scarification in children hospitalized in Congo]. *Med Trop (Mars)* 2011;**71**:509–10.

[12] Neequaye AR, Neequaye JE, Biggar RJ. Factors that could influence the spread of AIDS in Ghana, West Africa: knowledge of AIDS, sexual behavior, prostitution, and traditional medical practices. *J Acquir Immune Defic Syndr (1988)* 1991;**4**:914–19. doi:10.1097/00126334-199109000-00014.

[13] Centers for Diseases Control and Prevention, National Notifiable Diseases Surveillance System (NNDSS). Anthrax (Bacillus anthracis) 2018 case definition, https://ndc.services.cdc.gov/case-definitions/anthrax-2018/; 2018 [accessed 28 September 2023].

[14] Karahocagil MK, Akdeniz N, Akdeniz H, Çalka Ö, Karsen H, Bilici A, et al. Cutaneous anthrax in Eastern Turkey: a review of 85 cases. *Clin Exp Dermatol* 2008;**33**:406–11. doi:10.1111/j.1365-2230.2008.02742.x.

[15] Person MK, Cook R, Bradley JS, Hupert N, Bower WA, Hendricks K. Systematic review of hospital treatment outcomes for naturally acquired and bioterrorism-related anthrax, 1880–2018. *Clin Infect Dis* 2022;**75**:S392–401. doi:10.1093/cid/ciac536.

[16] Hendricks KA, Wright ME, Shadomy SV, Bradley JS, Morrow MG, Pavia AT, et al. Centers for Disease Control and Prevention expert panel meetings on prevention and treatment of anthrax in adults. *Emerg Infect Dis* 2014;**20**:e130687. doi:10.3201/eid2002.130687.

[17] Zasada AA. Injectional anthrax in human: a new face of the old disease. *Adv Clin Exp Med* 2018;**27**:553–8. doi:10.17219/acem/68380.

[18] Kaya A, Tasyaran MA, Erol S, Ozkurt Z, Ozkan B. Anthrax in adults and children: a review of 132 cases in Turkey. *Eur J Clin Microbiol Infect Dis* 2002;**21**:258–61. doi:10.1007/s10096-002-0704-6.

[19] Bravata DM, Holty JE, Wang E, Lewis R, Wise PH, McDonald KM, et al. Inhalational, gastrointestinal, and cutaneous anthrax in children: a systematic review of cases: 1900 to 2005. *Arch Pediatr Adolesc Med* 2007;**161**:896–905. doi:10.1001/archpedi.161.9.896.

[20] Romero-Alvarez D, Peterson AT, Salzer JS, Pittiglio C, Shadomy S, Traxler R, et al. Potential distributions of Bacillus anthracis and Bacillus cereus biovar anthracis causing anthrax in Africa. *PLoS Negl Trop Dis* 2020;**14**:e0008131. doi:10.1371/journal.pntd.0008131.

[21] Kutmanova A, Zholdoshev S, Roguski KM, Sholpanbay uulu M, Person MK, Cook R, et al. Risk factors for severe cutaneous anthrax in a retrospective case series and use of a clinical algorithm to identify likely meningitis and evaluate treatment outcomes, Kyrgyz Republic, 2005–2012. *Clin Infect Dis* 2022;**75**:S478–86. doi:10.1093/cid/ciac537.

[22] Bryskier A. *Bacillus anthracis* and antibacterial agents. *Clin Microbiol Infect* 2002;**8**:467–78. doi:10.1046/j.1469-0691.2002.00527.x.

[23] Chen Y, Succi J, Tenover FC, Koehler TM. Beta-lactamase genes of the penicillin-susceptible *Bacillus anthracis* Sterne strain. *J Bacteriol* 2003;**185**:823–30. doi:10.1128/JB.185.3.823-830.2003.

[24] Cavallo JD, Ramisse F, Girardet M, Vaissaire J, Mock M, Hernandez E. Antibiotic susceptibilities of 96 isolates of *Bacillus anthracis* isolated in France between 1994 and 2000. *Antimicrob Agents Chemother* 2002;**46**:2307–9. doi:10.1128/AAC.46.7.2307-2309.2002.

[25] Lee LV, Bower KE, Liang FS, Shi J, Wu D, Sucheck SJ, et al. Inhibition of the proteolytic activity of anthrax lethal factor by Aminoglycosides. *J Am Chem Soc* 2004;**126**:4774–5. doi:10.1021/ja0495359.

[26] Fridman M, Belakhov V, Lee LV, Liang FS, Wong CH, Baasov T. Dual effect of synthetic Aminoglycosides: antibacterial activity against *Bacillus anthracis* and inhibition of anthrax lethal factor. *Angew Chem Int Ed Engl* 2005;**44**:447–52. doi:10.1002/anie.200462003.