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Retrospective evaluation of 155 adult equids and 21 foals with tetanus in Western, Northern, and Central Europe (2000–2014). Part 1: Description of history and clinical evolution

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Abstract

Objective – To describe clinical data of hospitalized adult equids and foals with tetanus.
Design – Multicenter retrospective study (2000–2014).
Setting – Twenty Western, Northern, and Central European university teaching hospitals and private referral centers.
Animals – One hundred fifty-five adult equids (>6 months) and 21 foals (<6 months) with tetanus.
Interventions – None.
Measurements and Main Results – Information on geographic, annual and seasonal data, demographic- and management-related data, clinical history, clinical examination and blood analysis on admission, complications, treatments, and outcomes were described and statistically compared between adults and foals. The described cases were often young horses. In 4 adult horses, tetanus developed despite appropriate vaccination and in 2 foals despite preventive tetanus antitoxin administration at birth. Castration, hoof abscesses, and wounds were the most common entry sites for adults; umbilical cord infections and wounds for foals. Stiffness was the commonest observed initial clinical sign. Blood analyses frequently revealed an inflammatory response, hemoconcentration, muscle damage, azotemia, negative energy balance, liver damage, and electrolyte and acid base disturbances. Common complications or clinical signs developing during hospitalization included dysphagia, dyspnea, recumbency, hyperthermia, seizures, hyperlipemia, gastrointestinal impactions, dysuria, and laryngeal spasms. Cases were supported with wound debridement, antimicrobial treatment, tetanus antitoxin, muscle spasm and seizure control, analgesia, anti-inflammatory drugs, fluid therapy, and nutritional support. Mortality rates were 68.4% in adult horses and 66.7% in foals. Foals differed from adult horses with respect to months of occurrence, signalment, management-related data, potential causative events, clinical signs on admission, blood analysis, complications, and severity grades.
Conclusions – This is the first study that rigorously describes a large population of equids affected by tetanus. The information provided is potentially useful to clinicians for early recognition and case management of tetanus in adult horses and foals. Tetanus affects multiple organ systems, requiring broad supportive and intensive care. Neonatal and adult tetanus in the horse should be considered as distinct syndromes, as in human medicine.

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Keywords: *Clostridium tetani*, epidemiology, horses, infectious disease

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Abbreviation

TAT tetanus antitoxin

Introduction

Tetanus is a highly fatal disease in horses, with descriptions of the disease dating back to the time of Hippocrates.[1,2] The responsible bacterium, *Clostridium tetani*, and its toxins were isolated and characterized by the end of the 19th century. Subsequently successful passive immunization of horses against tetanus was introduced,[3,4] leading to a dramatic decrease in the incidence of this disease. Despite the fact that currently tetanus only occurs sporadically,[5] equine clinicians are still likely to encounter at least one case during their careers.[5,6] The significantly decreased exposure rate of veterinarians to tetanus emphasizes the need for detailed descriptions of recent cases to help clinicians with early disease recognition and up-to-date patient management, particularly in the face of the currently reported suboptimal vaccination rates in Europe.[7,8] An up-to-date descriptive overview of tetanus in the horse including details of the history and clinical progression of the disease is currently lacking. Most of the available literature generally only provides data on small numbers of cases or limited variables. Moreover, previous reports describe cases managed before 2000,[5,6,9–11] or do not reflect the current approach in equine medicine in Europe.[6,12,13] Disease progression, complication rates, and outcomes of recent cases may be different from earlier reports due to improvements in treatments, especially in developed countries. Furthermore, neonatal tetanus is considered a separate entity to adult tetanus in human medicine.[14] It is highly likely that equine neonates also have a different disease history and course compared to adults, yet none of the currently available studies describe the history, clinical features, or outcomes of tetanus in multiple foals.

The aims of this study were to describe in detail the history, clinical presentation, and progression of adult horses and foals affected by tetanus that were admitted to equine referral hospitals throughout Western, Northern, and Central Europe between 2000 and 2014.

Materials and Methods

Data collection

Through the Atypical Myopathy Alert Group Network[15] and the European College of Equine Internal Medicine, potential scientific collaborators were identified. The following criteria for collaborators were used: (1) located in Western, Northern, or Central Europe, (2) working in an academic equine referral center, or a large, private referral center with interest in scientific research, (3) working in a referral clinic where at least 1 equine internal medicine specialist (Diplomate ECEIM or ACVIM) is employed. At least 1 academic clinic was searched and contacted for every country. All collaborators who had diagnosed tetanus cases since the year 2000, and who agreed to collaborate in the study, received a case definition and a detailed, standardized data spreadsheet for specific variables to be retrospectively retrieved from the medical records. Subsequently, all data were collected, checked, and analyzed by the first author (G. van Galen).

Case definition

The following case inclusion criteria were used for this study: (1) cases with a clinical diagnosis of tetanus, (2) admitted to the referral hospital of a collaborator, (3) admitted between the years 2000 to 2014. Since no definitive diagnostic tests are available for tetanus, a clinical diagnosis of tetanus was based on the presence of the most typical and consistent clinical signs reported in the published literature (eg, stiffness, trismus, or protrusion of the third eyelid), and the absence of clinical signs, laboratory results and, where applicable, postmortem findings that indicated any other disease that could explain the clinical presentation.[16] Cases with the following findings were excluded from the study: (1) serum

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Claude Saegerman, Gaby van Galen, Joke Rijckaert, and Tim Mair were chosen according to the amount of work performed.

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The authors declare no conflict of interests.

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biochemical evidence of significant rhabdomyolysis (ie, creatine kinase activity of >10,000 U/L, or the presence of myoglobinuria), (2) hypocalcemia (ionized calcium < 1 mmol/L [2 mEq/L], total calcium < 2 mmol/L [4 mEq/L]), (3) signs and laboratory results suggestive of hepatic encephalopathy or significant liver damage (gamma-glutamyl transferase activity > 150 U/L), and (4) signs or result of complementary examinations suggestive of other neurological conditions.

Based on resemblance of the clinical parameters in foals older than 6 months and adults, and the fact that all foals should theoretically have received a first vaccination at this age, cases were divided into >6 months old (adults) and <6 months old (foals).

Retrieved data from reported cases and definitions

Detailed information about cases was retrieved retrospectively from the files with owner informed consent. For a minority of the cases no consent could be obtained because of absence of standard consent contracts on admission and unsuccessful attempts to reach the owner.

Geographic, annual, and seasonal data

The date of the first recognized clinical sign was recorded as well as the referral clinic and the country of the referral clinic.

Demographic and management related data

Breed, sex, age at the time of onset of disease, body condition (eg, normal, poor or obese), and exercise activity (eg, in training or in competition) were recorded. Cases were allocated into the following categories relating to tetanus vaccination: never vaccinated or correctly vaccinated according to the guidelines from the American Association of Equine Practitioners of a primary double vaccination with 4–6 weeks interval between doses and followed by a yearly booster.[17] In addition, the reason for not vaccinating was recorded. For foals it was noted if they had received tetanus antitoxin (TAT) after birth. It was noted whether cases were microchipped and dewormed.

Clinical history

The first clinical sign noted by the owner, any significant history prior to the onset of disease, entry sites or wounds, evidence of visible infection or necrosis at potential entry sites or wounds, and whether preventive TAT was administered following this event were noted. The distance from the home premises to the referral clinic was recorded in hours of travelling duration. The following dates were noted: date of the preceding significant event (if present; T1), date of development of the first clinical signs of tetanus (T2), date of the development of the first spasm (T3), date of clinical diagnosis of tetanus (T4), date of first treatment (excluding TAT; T5), date of first therapeutic treatment with TAT (T6), date of referral (T7), date of death (where appropriate; T8), date of start of clinical improvement (where appropriate; T9), date of complete clinical recovery (where appropriate; T10), and date of discharge from hospital (where appropriate; T11). Using these dates, the following intervals (in days) were calculated: incubation time (T1-T2), onset time (T2-T3), diagnosis time (T2-T4), treatment delay (T2-T5), TAT delay (T2-T6), hospitalization delay (T2-T7), disease length for nonsurvivors (T2-T8), period after which recovery starts (T2-T9), disease length for survivors (T2-T10), and hospitalization length (T7-T11 or T7-T8).

Table 1: Severity grades of tetanus for horses, adapted from Attygalle and Rodrigo, and Miranda-Filho et al[2,29]

Grade	Criteria
Mild	Mild-moderate trismus, general stiffness, no respiratory problems, no spasms, little or no dysphagia
Moderate	Moderate trismus, marked stiffness, mild-moderate short spasms, moderate respiratory embarrassment, mild dysphagia
Severe	Severe trismus, generalized stiffness, reflex prolonged spasms, respiratory embarrassment (respiratory rate >60/min), apneic periods, severe dysphagia, tachycardia (>60/min)
Very severe	Similar criteria as the severe grading, plus violent autonomic disturbances of cardiovascular system (severe hypertension and tachycardia alternating with hypotension and bradycardia)

Hospitalization

The results of blood analyses on admission or the first sampling time following admission were recorded. Complications or clinical signs that developed during hospitalization were recorded. Treatments were noted with specific emphasis on use of antimicrobials, TAT (eg, dosage, frequency, and administration route), muscle relaxants, analgesics, and fluid therapy and nutritional support. Grades of severity of tetanus (Table 1), the costs of the hospitalization, the final outcome (survivor or nonsurvivor), and results of postmortem examination were recorded.

Detailed data on outcome and prognostic factors are described in Part 2 of this study.[18]

Statistical methods

Adult cases and foals were compared by statistical analysis: 2-sample *t*-test with unequal variances for numerical

Table 2: Northern, Western, and Central European countries from where horses with tetanus were reported

Country	Total/country
Austria	8
Belgium	95
Czech Republic	7
Denmark	6
Finland	1
France	0*
Germany	12
Ireland	2
Norway	0*
The Netherlands	4
Spain	1
Sweden	18
Switzerland	9
United Kingdom	13
Total	177

Cases were categorized by the reporting referral clinic, not by physical location where they lived. A case could therefore be categorized as reported by Belgium but patient could have resided in the north of France.
*Absence of cases in the participating hospitals since the year 2000 or cases that were too poorly reported for use in this study.

variables, and Fisher's exact test for categorical variables. Significance was set at $P < 0.05$.

Results

In total, 185 cases were reported, of which 176 cases fulfilled the inclusion criteria for this study. Of those 176 cases, 120 were nonsurvivors and 56 were survivors, giving a survival rate of 31.8% and a mortality rate of 68.2%. Of these 176 cases, 155 were adult equids and 21 were foals younger than 6 months.

Geographic, annual, and seasonal distribution of cases

Cases were reported from 20 different referral clinics. The Universities of Ghent and Liege in Belgium reported most cases (71 and 20, respectively; Table 2). Annual distribution and seasonal distribution of the cases is illustrated in Figures 1 and 2, respectively. Peaks occurred in the months of April and December for adults, whereas cases in foals tended to occur in spring and summer.

Demographic- and management-related data

Cases had variable ages ranging from 6 days to 20 years, but most were young (4 years or younger). The majority of affected equids were saddle horses (ie, riding horses), of normal body condition, and not microchipped. Most were not being exercised. The adult and foal groups both showed an equal sex distribution. Two mares were pregnant. Very little data could be obtained on deworming history (response rate <25%). Most adults were never vaccinated, yet 4 were appropriately vaccinated (they were 1.5, 2.6, 4, and 13 years old at onset of disease). None of the foals had been vaccinated, but 2 received TAT at birth (they were 1 month and 6 days old at the onset of disease; Table 3). Vaccination status of the dams was unknown. Reasons given by the owners for not vaccinating were: ignorance (lack of knowledge about tetanus or appropriate vaccination regimen); postponed due to housekeeping/practical problems; advice from horse dealer; the foal was too young, and the dam was not vaccinated; purchased recently and no information on vaccination status available; vaccination costs too high; no previous problems with a nonvaccination strategy.

Clinical history

For one third of the adults and the foals, a specific event was noted that potentially could have caused tetanus. Castration, hoof abscesses, and wounds were the most common events for adults, whereas in foals preceding events were only umbilical cord infections or wounds. Prophylactic administration of TAT following these events was only undertaken in 10 adult cases and not in any of the foals (Table 4).

Disease intervals were quite similar for both groups (Table 5). Incubation times were variable with a mean of 1 week. Onset time, diagnosis time, treatment delay, TAT delay, and hospitalization delay were usually within 24 hours of the onset of disease.

Hospital admission

Stiffness was reported by the owner as the most commonly observed initial clinical sign. The clinical signs recorded at admission to the hospitals are summarized in Table 6. Not all cases showed all of the signs of the study definition of tetanus (eg, stiffness, third eyelid protrusion, trismus) on admission, but they had at least 1 of the 3 signs on admission and developed the other signs later in the course of the disease. Trismus was frequently not present on the day of admission. Common clinical signs identified early in the course of the disease in more than 50% of adult horses were: stiffness, third eyelid protrusion, trismus, agitation, wide-based stance, extended neck, elevated tail, dysphagia, anorexia, abnormal (decreased or absent) intestinal sounds, and abnormal (decreased or absent) defecation. In foals, common clinical signs identified early in the course of the disease were slightly different and included: stiffness, third eyelid protrusion, recumbency, muscle spasms, extended neck, abnormal (decreased or absent) defecation, and abnormal (decreased or absent) urination. The majority of foals and adults additionally had normal mucous membranes, normal rectal temperature, tachycardia, and tachypnea, although congested mucous membranes, low or normal

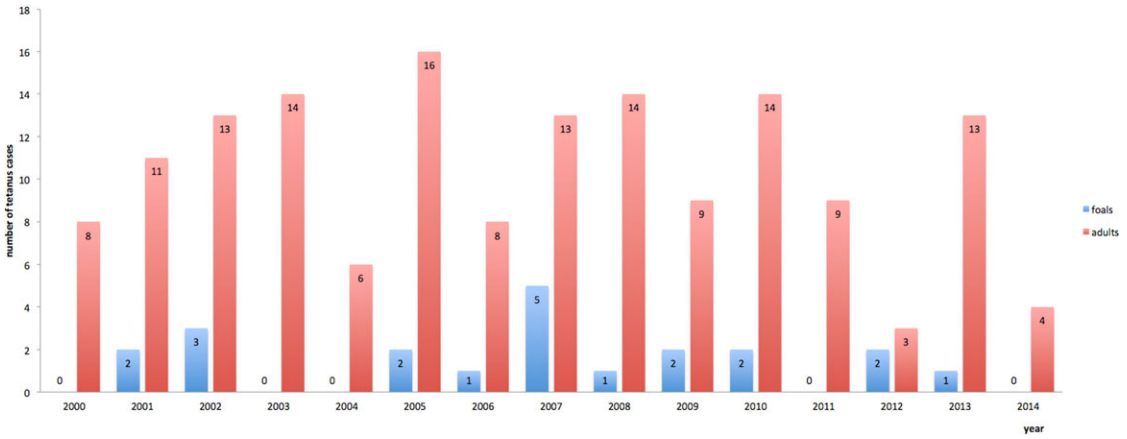

Figure 1: Annual distribution of adult horses and foals with tetanus. The year of disease of a case was based on the date of the first clinical sign or, if that date was unknown, on the date of hospitalization.

heart rates, normal respiratory rates, hypothermia, and hyperthermia also occurred regularly. Five horses were reported to have arrhythmias on cardiac auscultation.

A small group of horses was euthanized on or immediately after admission without initiation of treatment: 10 adults (of which 4 were euthanized for financial reasons; the other 6 had moderate [1] and severe grading [5]) and 2 foals (none for financial reasons, but with severe [1] and very severe grading [1]).

Hospitalization and outcome

The results of blood analyses most frequently revealed evidence of an inflammatory response, hemoconcentration, muscle damage, azotemia, negative energy balance, liver damage, electrolyte disturbances, and metabolic and respiratory acid base disturbances (Table 7). In only 2 cases a bacterial culture was performed of the wound, and in one of these C *tetani* was cultured.

Cases were treated with wound debridement (91% of the cases with a wound), penicillin (75.8% intravenously and 21.3% intramuscularly), metronidazole (8.3%), and other antimicrobials with or without penicillin (45.2%). Furthermore, 97.6% received therapeutic doses of TAT, of which the majority was administered intravenously (89.3%) with a total dose of 5,000–600,000 IU (mean 80,374 ± 69,070 IU) divided over 1–9 injections. A single atlanto-occipital intrathecal TAT administration was performed in 16 adults cases with a dosage of 8,000–58,000 IU (mean 35,173 ± 14,943 IU). One horse was reported to collapse during intrathecal TAT administration. Twelve of those 16 did not survive tetanus. Four adults, of which 2 survived, did not receive any TAT. Several drugs, such as acepromazine (87%), diazepam (39.7%), midazolam (2.1%), alpha$_2$-adrenergic agonists (27.4%), glycerol guaiacolate (16.4%), magnesium (3.4%), methocarbamol (2.7%), dantrolene (2.1%), and barbiturates (0.7%),

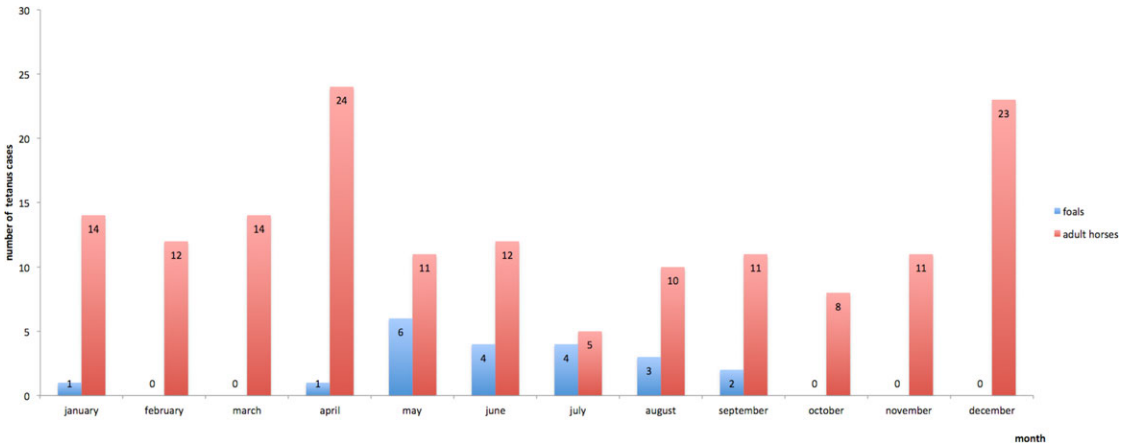

Figure 2: Seasonal distribution of adult horses and foals with tetanus. The month of disease of a case was based on the date of the first clinical sign or, if that date was unknown, on the date of hospitalization.

Table 3: Demographic- and management-related data of foals and adult horses with tetanus

	Adult horses (155)			Foals (21)			
Age (years)							#
Mean ± SD	4.2 ± 3.8			0.2 ± 0.2			
Median	3.0			0.10			
Range	0.6–20.0			6 days–6 months			
N	152			17			
	n	***N***	**%**	***n***	***N***	**%**	
Breed							
Pony	20	152	13.2	6	21	28.6	
Donkey	7	152	4.6	0	21	0.0	
Draft horse	11	152	7.2	2	21	9.5	
Saddle horse	114	152	75.0	13	21	61.9	
Sex							
Mare	89	154	57.8	10	21	47.6	
Gelding	36	154	23.4	1	21	4.8	#
Stallion	29	154	18.8	10	21	47.6	#
Body condition							
Normal	115	130	88.5	18	21	85.7	
Poor	11	130	8.5	3	21	14.3	
Obese	4	130	3.1	0	21	0.0	
Exercise activity							
In training	13	110	11.8	0	21	0.0	
In competition	1	107	0.9	0	21	0.0	
Tetanus immunization							
Never vaccinated	72	109	66.1	18	20	90.0	#
Correctly vaccinated*	4	106	3.8	0	19	0.0	
TAT after birth**	-	-	-	2	16	12.5	
Microchipped	29	103	28.2	0	19	0.0	#

N, number of horses with a response for this specific parameter; *n*, number of horses with a positive response.

*According to the guidelines from the American Association of Equine Practitioners of a primary double vaccination with 4- to 6-week interval between doses and followed by a yearly booster.[17]

**Only recorded for foals.

#Variable statistically different between groups.

were used to control muscle spasms. Nonsteroidal anti-inflammatory drugs (32.9%), morphine or morphine derivatives (4.8%), a continuous rate infusion of lidocaine (2.1%), and dimethyl sulphoxide (2.8%) were used as analgesic or anti-inflammatory therapies. Despite the fact that about half of the cases (58.5%) were able to drink, intravenous (85.6%) or oral (21.9%) fluid therapies were used frequently to provide cardiovascular support. Voluntary eating of normal or softened food was possible for 27.0% and 39.4% of cases, respectively. Tube feeding, intravenous administration of glucose, and parenteral nutrition were utilized to provide nutritional support in 15.7%, 47.6%, and 1.4%, respectively. Most cases were placed in a darkened (97.9%), padded (78.6%), and silent (97.9%) stable to reduce stimuli-induced muscle spasms and seizures, and in some cases a sling was used (30.7%).

Complications or clinical signs that developed during hospitalization and which reporting veterinarians were specifically questioned about are shown in Table 8. Commonly dysphagia, dyspnea, recumbency, hyperthermia, seizures, hyperlipemia, gastrointestinal impactions, dysuria, and laryngeal spasms were encountered during hospitalization. In addition to the standardly questioned ones, the following complications or clinical signs were reported: apnea (5), laminitis or increased digital pulses (4), pulmonary edema (3), opisthotonus (3), inflammation at an intramuscular injection site (1), severe head and neck edema (1), abortion (1), photophobia (1), corneal ulcers (1), contracted carpi and fetlocks (1 foal), cecal impaction with subsequent rupture (1). For both age groups, cases were mainly categorized as mild, moderate or severe, and very severe cases were rare (Table 9).

Mortality rates were similar in both groups: 68.4% (106/155) in adults and 66.7% (14/21) in foals. Only 12 nonsurvivors died after more than 7 days of the onset of clinical disease; the remainder died within the first week. Twenty-four adult cases and 4 foals underwent a full postmortem examination. None of them had gross lesions that could explain the clinical syndrome. Additionally, gastrointestinal parasites were found in 35% (7/20) of the adult horses undergoing postmortem examination, 1 had a rupture of the femoral head ligament, and 6 had muscle lesions (eg, local myositis, fiber degeneration, muscle tearing, hemorrhage).

The survival rates of the adults and foals were 31.6% (49/155) and 33.3% (7/21), respectively. Initial signs of clinical improvement were typically seen after >1 week after the onset of disease, with full recovery commonly occurring within 3 weeks. Nine adult horses and 1 foal were discharged before full recovery from tetanus (Table 5). The average hospitalization time was 9–10 days (Table 5) with an associated cost of € 902 ± 784 for adults ($n = 130$) and € 835 ± 947 for foals ($n = 18$).

Statistical comparison between adult horses and foals with tetanus

Variables more associated with adults compared to foals included: gelding, microchipped, presence of a wound, third eyelid protrusion, trismus, wide-based stance, elevated tail, dysphagia and normal urination on admission, and moderate disease grading. Variables more associated with foals compared to adults included: stallion, never vaccinated, no event noted that could be at the origin of the disease, generalized seizures and recumbency on admission, development of increased rectal temperatures during hospitalization, and very severe disease grading. Moreover, foals had a significantly higher heart rate, respiratory rate, rectal temperature, white blood cell count, blood sodium, and ionized calcium concentration on admission, but a significantly lower serum

Table 4: Variables from the clinical history of adult horses and foals with tetanus

	Adult horses (155)			Foals (21)			
	n	***N***	**%**	***n***	***N***	**%**	
Event before tetanus development							
No event noted	72	154	46.8	15	21	71.4%	#
Castration	11	154	7.1	0	21	0.0%	
Other surgery	3	154	1.9	0	21	0.0%	
Hoof abscess	14	154	9.1	0	21	0.0%	
Dental floating	1	154	0.6	0	21	0.0%	
Retained placenta (mares)	0	154	0.0	–	–	–	
Umbilical cord infection (foals)	–	–	–	3	21	14.3%	
Wound	59	154	38.3	3	21	14.3%	#
Visual inspection wound							
Infection	29	57	50.9	4	6	66.7%	
Necrosis	10	51	19.6	0	5	0.0%	
Preventive TAT in relation to event	10	74	13.5	0	6	0.0%	

N, number of horses with a response for this specific parameter; *n*, number of horses with a positive response; TAT, tetanus antitoxin.
[#]Variable statistically different between groups.

total protein concentration, creatinine concentration, and gamma-glutamyl transferase activity than adult cases (Tables 3–9).

Discussion

To the best of the authors' knowledge, this is the first study that rigorously describes a large European population of horses affected by tetanus. This study provides clinicians with an evidence-based description of the clinical disease, which is useful not only in regards to recognizing and diagnosing the disease, but also with treatment, prevention of complications, and prognosis. In agreement with previous reports,[5] stiffness was the most consistently recognized early sign of the disease in the present study. Protrusion of the third eyelid and trismus developed later in the course of the disease, especially in foals, which potentially might complicate early recognition of the disease since these signs have been described as key features of tetanus.[16]

Analyzing the most common clinical signs, results of blood analyses and complications associated with tetanus, clinicians should recognize that the disease affects multiple organ systems, requiring broad supportive and often intensive care. Treatments should focus on support of the respiratory and cardiovascular systems, the gastrointestinal tract (including nutritional support), the urinary system, and metabolic functions. Moreover, traumatic complications as result of violent contractions or seizures, such as fractures, muscle or ligament trauma, decubital ulcers, and corneal ulcers, can occur and clinicians should attempt to avoid these with proper care of recumbent horses and control of seizures and muscle spasms. A small number of horses were graded as very severe with reference to autonomic disturbances. This number is likely to be underreported

Table 5: Disease intervals of adult horses and foals with tetanus

	Adult horses (155)				Foals (21)			
	Mean ± SD	***M***	***R***	***N***	**Mean ± SD**	***M***	***R***	***N***
Incubation time (days)	10.8 ± 7.3	8.0	1–43	49	6.0	6.0	6.0	1
Onset time (days)	0.5 ± 1.3	0.0	0.0–12	135	0.3 ± 0.8	0.0	0.0–3.0	21
Diagnosis time (days)	1.2 ± 2.5	0.5	0.0–19	144	0.9 ± 1.6	0.0	0.0–5.0	21
Treatment delay (days)	1.2 ± 2.6	0.5	0.0–19	140	0.8 ± 1.5	0.0	0.0–5.0	19
TAT delay (days)	1.2 ± 2.6	0.5	0.0–19	137	0.8 ± 1.5	0.0	0.0–5.0	19
Transport time (hours)	1.5 ± 1.0	1.0	0.5–7.5	77	1.2 ± 0.7	1.0	0.5–3.0	10
Hospitalization delay (days)	1.4 ± 2.8	0.5	0.0–19	143	1.1 ± 1.9	0.1	0.0–6.0	21
Disease length for NS (days)	4.2 ± 5.5	3.0	0.0–38	103	3.6 ± 4.2	2.0	0.0–16	14
Period after which recovery starts (days)	8.5 ± 5.3	8.0	2.0–21	38	8.7 ± 3.3	10.0	3.0–12	7
Disease length for S (days)	19.6 ± 6.7	20.5	5.0–33	34	21.0 ± 16.2	17.0	7.0–53	6
Hospitalization length (days)	8.9 ± 10.7	3.5	0.0–52	155	10.1 ± 13.5	3.7	0.0–56	21

SD, standard deviation; M, median; *R*, range; *N*, number of horses with a response for this specific parameter; NS, nonsurvivor; S, survivor; TAT, tetanus antitoxin.

Table 6: Clinical signs on admission of adult horses and foals with tetanus

	Adult horses (155)			Foals (21)			
	n	***N***	**%**	***n***	***N***	**%**	
Case definition signs							
Stiffness	151	155	97.4	21	21	100	
Third eyelid protrusion	139	150	92.7	15	21	71.4	#
Trismus	93	148	62.8	8	21	38.1	#
Mental status—consciousness							
Normal	31	143	21.7	3	21	14.	
Depressed	42	140	30.0	8	21	38.1	
Generalized seizures	9	140	6.4	6	20	30.0	#
Agitated	75	138	54.3	7	20	35.0	
Anxious	48	137	35.0	5	20	25.0	
Other neurological signs							
Recumbency	18	155	11.6	13	21	61.9	#
Involuntary muscle contractions/spasms	63	148	42.6	12	20	60.0	
Wide-based stance	74	142	52.1	2	19	10.5	#
Retracted lips	37	123	30.1	2	20	10.0	
Pulled down ears	44	129	34.1	3	18	16.7	
Extended neck	81	136	59.6	11	20	55.0	
Elevated tail	92	136	67.6	5	19	26.3	#
Dysphagia	81	138	58.7	4	18	22.2	#
Clinical examination							
Heart rate (bpm)							#
Mean ± SD	63.1 ± 18.0			97.0 ± 26.1			
Median	60			100			
Range	32–120			60–148			
N	142			18			
Respiratory rate (bpm)							#
Mean ± SD	42.7 ± 24.3			70.0 ± 38.1			
Median	36			64			
Range	8–120			20–160			
N	124			19			
Rectal temperature (°C)							#
Mean ± SD	37.8 ± 0.8			38.6 ± 0.8			
Median	37.8			38.8			
Range	35.6–40.8			36.2–39.6			
N	121			17			
Normal mucous membranes	87	133	65.4	12	18	66.7	
Dyspnea	58	129	45.0	9	20	45.0	
Normal intestinal sounds	41	93	44.1	6	10	60.0	
Normal defecation	39	85	45.9	3	10	30.0	
Anorexia	71	130	54.6	8	19	42.1	
Signs of colic	18	145	12.4	0	21	0.0	
Normal urination	53	62	85.5	4	8	50.0	#
Sweating	59	144	41.0	6	19	31.6	

N, number of horses with a response for this specific parameter; *n*, number of horses with a positive response; bpm, beats/breaths per minute; #, variable statistically different between groups.

since measurements of autonomic parameters (such as blood pressure and continuous heart rate monitoring) are rarely systematically undertaken in equine medicine. However, the relative bradycardia in some horses in this study in the face of painful muscle cramps and the severe tachycardia in others are suggestive of autonomic dysfunction. This phenomenon of autonomic disturbances is well described in people[2] and dogs[19,20] suffering from tetanus, but this is the first time it has been reported in horses.

Despite the comparable survival rates compared to previous reports in the published literature, some differences can be noted with regards to complications. In the study from Muylle with 108 cases, the only complication described was aspiration pneumonia.[11] This complication only developed in 2 adult horses and 2 foals in the

Table 7: Blood analysis of adult horses and foals with tetanus

	Adult horses (155)					Foals (21)				
	Ref range*	**Mean ± SD**	***M***	***R***	***N***	**Mean ± SD**	***M***	***R***	***N***	
PCV L/L (%)	0.30–0.45 (30–45)	0.361 ± 0.87 (36.1 ± 8.7)	0.36 (36.0)	0.20–0.59 (20–59)	132	0.355 ± 0.039 (35.5 ± 3.9)	0.35 (35)	0.30–0.45 (30–45)	18	
WBC* ($\times 10^9$/L)	6–14	10.0 ± 3.5	9.6	4.7–20.0	65	16.5 ± 5.6	14.6	11.0–27.5	11	#
CK (U/L)	119–287	1184 ± 1908	382	84–8480	49	1247 ± 1186	987	50–3558	7	
Triglycerides mmol/L (mg/dL)	<1.13 (<100)	1.48 ± 1.2 (131.2 ± 107.0)	1.2 (106)	0.3–5.4 (26.3–481)	15	–	–	–	0	
Glucose mmol/L (mg/dL)	5–6.2 (89–112)	8.0 ± 3.3 (144.8 ± 59.3)	7.5 (135)	3.0–18.0 (54–324)	29	6.8 ± 1.9 (122.3 ± 34.5)	6.0 (108)	5.0–11.0 (90–198)	9	
Total protein g/L (g/dL)	58–77 (5.8–7.7)	68.7 ± 9.4 (6.87 ± 0.94)	69.4 (6.94)	48–98 (4.8–9.8)	65	61.2 ± 4.6 (6.12 ± 0.46)	61.5 (6.15)	54–68 (5.4–6.8)	10	#
Albumin g/L (g/dL)	23–36 (2.3–3.6)	30.6 ± 4.5 (3.06 ± 0.45)	30.0 (3.0)	24–54 (2.4–5.4)	27	29.7 ± 4.1 (2.97 ± 0.41)	30.4 (3.04)	22–33 (2.2–3.3)	6	
Total bilirubin μmol/L (mg/dL)	8.6–39.3 (0.5–2.3)	41.0 ± 29.1 (2.4 ± 1.7)	34.2 (2.0)	5.1–118.0 (0.3–6.9)	28	49.6 ± 27.4 (2.9 ± 1.6)	(2.9)	30.8–68.4 (1.8–4.0)	2	
Urea mmol/L (mg/dL)	4.3–9.6 (12–27)	8.6 ± 5.2 (24.2 ± 14.7)	7.1 (19.9)	1.3–32.1 (3.6–90.0)	37	7.0 ± 2.3 (19.7 ± 6.5)	5.9 (16.5)	5.1–11.6 (14.3–32.5)	7	
Creatinine μmol/L (mg/dL)	80–177 (0.9–2.0)	177 ± 230 (2.0 ± 2.6)	115 (1.3)	62–1467 (0.7–16.6)	41	97 ± 35 (1.1 ± 0.4)	106 (1.2)	44–150 (0.5–1.7)	8	#
GGT (U/L)	8–22 (foals <50)	30.9 ± 30.5	19.0	9–145	31	17.0 ± 9.3	17	8–26	4	#
Na mmol/L or mEq/L	134–142	135.9 ± 5.0	136	121–149	64	139.3 ± 4.7	139	131–146	11	#
Cl mmol/L or mEq/L	97–104	99.4 ± 5.2	99	88–112	31	102.2 ± 5.2	102	94–109	9	
K mmol/L or mEq/L	3.5–4.6	3.6 ± 0.4	3.5	2.8–4.7	64	3.5 ± 0.4	3.6	2.6–3.9	12	
Total calcium mmol/L (mEq/L)	2.8–3.4 (5.6–6.8)	2.8 ± 0.3 (5.6 ± 0.6)	2.8 (5.6)	2.4–3.7 (4.8–7.4)	20	2.9 ± 0.1 (5.8 ± 0.2)	2.9 (5.8)	2.7–3.0 (5.4–6.0)	4	

(Continued)

Table 7: *(Continued)*

	Adult horses (155)					Foals (21)				
	Ref range*	**Mean ± SD**	***M***	***R***	***N***	**Mean ± SD**	***M***	***R***	***N***	
Ionized calcium mmol/L (mEq/L)	1.45–1.73 (2.9–3.5)	1.4 ± 0.1 (2.8 ± 0.2)	1.4 (2.8)	1.2–1.7 (2.4–3.4)	39	1.5 ± 0.1 (3.0 ± 0.2)	1.6 (3.2)	1.2–1.6 (2.4–3.2)	7	#
Lactate mmol/L (mg/dL)	<2 (<18)	6.0 ± 5.0 (54 ± 45)	5.2 (47)	1.5–20 (13.5–180)	18	5.5 ± 2.5 (50 ± 22.5)	6.4 (57.7)	1.4–8.2 (12.6–73.9)	6	
pH	7.31–7.45	7.37 ± 0.06	7.38	7.22–7.48	54	7.40 ± 0.06	7.38	7.30–7.50	13	
Bicarbonate (mmol/L or mEq/L)	24–30	24.7 ± 4.5	25.6	15.3–32.9	58	25.4 ± 4.8	27.2	14.0–31.6	12	
BE (mmol/L)	-5 - +5	0.7 ± 5.2	1.35	-10.9 to 11.9	80	1.2 ± 4.6	2.3	-8.0 to 7.6	17	
$pvCO_2$ (mm Hg)	41–53	45.2 ± 6.6	44.4	27.4–60.4	53	45.6 ± 4.9	46.1	37.5–51.8	10	

*Data from reference.[30]

#Variable statistically different between groups.

SD, standard deviation; *M*, median; *R*, range; *n*, number of horses with a response for this specific parameter; PCV, packed cell volume; WBC, white blood cell count; CK, creatine kinase activity; GGT, gamma-glutamyl transferase; Na, sodium; Cl, chloride; K, potassium; BE, base excess; $pvCO_2$, venous partial pressure of carbon dioxide.

Table 8: Complications and clinical signs that developed during hospitalization in adult horses and foals with tetanus

	Adult horses (155)			Foals (21)			
	N	***n***	**%**	***N***	***n***	**%**	
Dysphagia	97	136	71.3	9	19	47.4	
Recumbency	77	143	53.8	13	19	68.4	
Dyspnea	73	141	51.8	8	19	42.1	
Increased rectal temperature (>38.5°C)	31	127	24.4	13	19	68.4	#
Seizures	28	142	19.7	6	19	31.6	
Hyperlipemia	9	89	10.1	0	14	0.0	
Gastrointestinal impaction	12	135	8.9	3	17	17.6	
Weight loss	9	112	8.0	0	17	0.0	
Dysuria	10	132	7.6	2	19	10.5	
Laryngeal spasms and/or stridor	10	135	7.4	2	19	10.5	
Decubital ulcers	8	141	5.7	0	19	0.0	
Thrombophlebitis	7	143	4.9	1	19	5.3	
Diarrhea	6	143	4.2	1	19	5.3	
Bone fractures	5	143	3.5	0	19	0.0	
Gastrointestinal distension	3	139	2.2	0	19	0.0	
Aspiration pneumonia	2	128	1.6	2	18	11.1	
Renal failure	2	131	1.5	0	19	0.0	

#, variable statistically different between groups

Table 9: Severity grades of adult horses and foals with tetanus

	Adult horses (155)			Foals (22)			
	N	***n***	**%**	***N***	***n***	**%**	
Mild	35	155	22.6	6	21	28.6	
Moderate	70	155	45.2	4	21	19.0	#
Severe	47	155	30.3	8	21	38.1	
Very severe	3	155	1.9	3	21	14.3	#

Explanation of the severity grades can be found in Table 1.
#Variable statistically different between groups.
N, number of horses with a positive response; n, number of horses with a response for this specific parameter.

current study. Comparatively, a larger number of other complications were reported in the present study, which can be explained by the increased accessibility to laboratory facilities for monitoring blood analyses, and the study design where reporting veterinarians were specifically questioned on complications. Most common complications or clinical signs that developed during hospitalization in the present study were dysphagia, dyspnea, recumbency, hyperthermia, seizures, hyperlipemia, gastrointestinal impactions, dysuria, and laryngeal spasms.

In addition to reporting on tetanus in adult horses, the present study also describes the features of the disease in a group of foals. Differences were recognized between the groups with reference to the months of occurrence, signalment, management-related data, potential causative events, clinical signs on admission, blood analysis, complications, and severity grades. Therefore, we suggest that similar to the situation in human medicine, tetanus in foals and tetanus in adult horses should be considered as distinct syndromes. However, there was no observable difference between groups for survival rate and disease intervals.

This study indicates that cases of tetanus are uncommon in most Western, Northern, and Central European referral clinics, except for the University of Ghent and of Liege, both located in Belgium. The number of cases per country in this study is certainly an underestimation of the true number of cases. Although this study was not designed to study the incidence of tetanus, it does suggest that case numbers seem relatively stable over the last 15 years. It is reasonable to expect that most foals would be affected from April to September, but it is unclear why a peak in adult cases occurs in April and December. The case numbers also suggest some differences between countries. The large difference in case numbers between Belgium and the other European countries theoretically could either be due to lower rates of immunization, or different degrees of exposure of horses to *Clostridium tetani* through diversity of soil contamination. *Clostridium tetani* is believed to be commonly present in the soil, but geographical differences have been observed; for example, total absence of this bacterium has been identified in the soils of the Rocky Mountains and the Andes Mountains.[1] Moreover, outbreaks of tetanus have been reported following events that result in significant environmental soil contamination, such as following earthquakes and tsunamis.[21–23] It is unclear whether the vaccinated horses that developed tetanus in this study did so as a result of exposure to a particularly high infection pressure. They could, however, be a consequence of lower immunization rates.

In Belgium, the annual American Association of Equine Practitioners vaccination scheme[17] is routinely used, so increased tetanus case numbers cannot be attributed to vaccination schemes with longer booster intervals. Other reasons why vaccinated horses could develop tetanus include: poor immune response of the horse to the vaccine, the owner not admitting that the horse was inappropriately vaccinated, vaccination with an inappropriate administration of the vaccine or an inappropriately stored vaccine.

Only a small number of wounds in the horses affected by tetanus in this study were assessed for bacterial contamination or the presence of *Clostridium tetani*. Although the organism cannot be recovered in 46–70% of human cases with anaerobic culture methods,[1,24] a Gram stain can aid in identification of *C tetani* [1,25] Attempts to culture *C tetani* from possible entry wounds can help to confirm the diagnosis of tetanus, which is currently in most equine cases restricted to identification of the typical clinical signs. Furthermore, knowledge on the bacterial flora and antimicrobial susceptibility patterns of infected entry wounds can be helpful to optimize wound treatments. In two thirds of the described cases, no potential entry site was detected. *Clostridium tetani* requires anaerobic conditions in order to multiply and produce its toxin, so it is likely that entry wounds are frequently small stab wounds that rapidly heal. Consequently, they can be easily missed under the hair coat. One result of particular note was the observation that castration and hoof abscesses were the most common predisposing events for the development of tetanus in this group of horses; this highlights the importance of undertaking appropriate vaccination prior to performing elective surgical procedures and TAT or booster vaccination in case of hoof abscesses. *Clostridium tetani* is also a common inhabitant of the gastrointestinal tract of horses [26] and, similar to the situation in people, intestinal lesions are likely to be a potential entry site for the bacterium in horses.[27,28] Unfortunately in the present study insufficient data were gathered on deworming protocols and parasitic lesions on postmortem examinations to study a possible relation between parasitic infestations and the development of tetanus.

Limitations of this study include its retrospective nature and the large number of reporting clinicians. However, potential bias was limited by the use of standardized data collection sheets, and the high response rate for most variables in this study.

In conclusion, this study provides a current review of the clinical features of a large number of tetanus cases, both in adult horses and foals in Western and Central Europe. The results provide clinicians with important information about the history, early clinical signs, laboratory results, clinical progression, and complications of the disease. This information should aid clinicians to achieve early diagnosis and provide good case management of this uncommon, yet serious condition affecting multiple organ systems, and requiring broad supportive and intensive care. Neonatal and adult tetanus in the horse should be considered as distinct syndromes, as in human medicine.

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