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Epidemiological characteristics of brucellosis in Vojvodina, Serbia, 2000–2014

Epidemiološke karakteristike bruceloze u Vojvodini, Srbija, 2000–2014

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Abstract

Background/Aim. Despite the fact that brucellosis occurs sporadically in the epidemic form, this disease is still one of the world's most widespread zoonoses. Methods. Data from the register of infectious diseases of the Institute of Public Health of Vojvodina and Scientific Veterinary Institute in Novi Sad were used in this study. Using descriptive statistics, data were analyzed for the period 2000 to 2014. Results. In the observed period in Vojvodina 102 cases of brucellosis were registered with different frequency of notification cases by districts of province. Most frequent modes of transmission of brucellosis were consumption of contaminated food (especially sheep cheese) or direct contact with domestic animals. In 70.2% of the patients, occupational exposures to the agent or direct daily contact with animals were noted. The dominant source of infection in the urban area was food, whereas a direct contact with sick animals was dominant mode of transmission in the rural area. Overall, 14 epidemic outbreaks of brucella were registered with direct contact as dominant mode of transmission. The predominant age-range of patients with brucella confirmed infections was 30-59 years (50.0 male %), and 2.5 times more males than females were affected. Seasonal distribution was highest during spring, with 50.0% of all confirmed cases. During the period 2004-2005, prevalence of serum positive patients in the South Bačka District coincided with the highest number of laboratory confirmed serum samples among animals. Conclusion. Although the incidence of brucellosis shows a declining trend, education and improving of surveillance of disease of all relevant institutions seems as necessary for better recognition and notification of the disease.

Key words:

brucellosis; serbia; disease outbreaks; disease transmission, infectious; infection control.

Apstrakt

Uvod/Cilj. Uprkos činjenici da se bruceloza sporadično registruje u epidemijskoj formi, ona i dalje predstavlja jednu od najraširenijih zoonoza u svetu. Metode. Podaci za istraživanje dobijeni su iz registra infektivnih bolesti Instituta za javno zdravlje Vojvodine i Veterinarskog instituta u Novom Sadu. Upotrebom deskriptivne statistike, analizirani su podaci za period 2000-2014. godina. Rezultati. U posmatranom periodu u Vojvodini je registrovano 102 slučaja bruceloze sa različitom učestalošću registrovanih slučajeva u odnosu na okruge pokrajine. Najčešći putevi širenja bruceloze su bili konzumiranje inkriminisane hrane (posebno ovčiji sir) ili direktni kontakt sa domaćim životinjama. Profesionalna izloženost agensu ili direktan dnevni kontakt sa životinjama naveden je kod 70,2% bolesnika. Dominantan izvor infekcije u gradskim naseljima bila je hrana, dok je u ruralnim delovima direktan kontakt sa bolesnim životinjama bio najčešći put prenosa infekcije. Registrovano je 14 epidemija bruceloze usled direktnog kontakta kao dominantnog puta širenja infekcije. Najveće učešće među potvrđenim slučajevima bruceloze bilo je u uzrastu 30-59 godina (50%), a oboljenje je 2,5 puta češće registrovano kod muškarca nego kod žena. Od ukupnog broja obolelih, 50% slučajeva oboljenja registrovano je tokom proleća. Tokom 2004. i 2005. godine, prevalencija pozitivnih seruma među bolesnicima u Južnobačkom okrugu koincidirala je sa najvećim brojem laboratorijski potvrđenih pozitivnih seruma među životinjama. Zaključak. Iako je trend bruceloze u opadanju, čini se da su edukacija i unapređenje nadzora nad oboljenjem svih relevantnih institucija neophodni za njegovo bolje prepoznavanje i registraciju.

Ključne reči: bruceloza; srbija; epidemije; infekcija, putevi širenja; infekcija, kontrola.

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Introduction

Brucellosis is a disease that originates from the anthropozoonosis group. It is primarily an occupational disease that predominantly affects people who are employed on farms, work with infected animals, veterinarians and slaughterhouse workers. The disease occurs sporadically in the epidemic form. The most common source of the infection is aborted material of the infected animals and their secretions. Brucellosis is transmitted by direct skin contact or mucous of the infected animals, by animal's offspring, amniotic fluid, and their urine and through inhalation of aerosols indoors where animals stay. Alimentary mode of transmission due to consumption of dairy products of raw milk is a predominant mode of spreading the infection in general population and most often comes from raising animals that are not registered ¹.

The causative agents of the disease are bacteria of the genus *Brucella*. Types of *Brucella* that cause human disease are: *B. melitensis* – primary hosts are sheep and goats; *B. abortus* – primary hosts are cattle; *B. suis*, biotype 3, the primary host is the pig, and *B. canis* – primary host is the dog 2 .

Nonspecific or atypical course of the disease in humans makes confirmation of diagnosis difficult. The clinical features are usually dominated by fever, headache, sweating, chills, arthralgia, depression, weight loss with pain throughout the body. Duration of the disease depends on the timely recognition of the disease diagnosis and adequate treatment, which can last several days, up to a year, or even longer ³.

The clinical manifestations of the disease in sheep are abortions, retention of placenta, orchitis, epididymitis and changes on the joints. The abortion in sheep, being the most common clinical manifestation of the disease, usually occurs once and is followed by autosterilization for a period from 6 months to one year. However, a certain number of animals remains carriers which retain the infection in the herd. Unlike sheep, in which spontaneous healing is observed relatively often, goats remain infectious throughout life. Brucellosis can spread in the herd during the two periods – the mating period and the lambing period. The diagnosis of disease among animals is made on the basis of epizootic data, clinical presentation, pathomorphological findings, epidemiological investigations and laboratory tests ⁴.

Considering that this disease in humans is often underdiagnosed or underestimated, and that in animals the form is usually non-clinical infection, the true frequency and distribution of brucellosis are unknown neither in humans nor in animals⁵.

The aim of this study was to determine the epidemiological characteristics of brucellosis in the Autonomus Province (AP) of Vojvodina, Serbia, and epizootiological characteristics in the South Bačka District in the period of 15 years, from 2000 to 2014.

Methods

The AP of Vojvodina is located in the northern part of Serbia and is divided into 7 districts and 44 municipalities. As a source of data we used the database from the register of infectious diseases of the Centre for Disease Control and Prevention of the Institute for Public Health (IPH) of Vojvodina, data of laboratory results of the Centre for Microbiology of the IPH and data of the Scientific Veterinary Institute in Novi Sad.

Information about individual cases of brucellosis in humans and data about patients in epidemics were analyzed on the basis of the notifications about infectious diseases and epidemiological data obtained by interviewing patients, on the data of the official monthly and annual reports of the IPH of Vojvodina in the period from 2000 to 2014. The incidence rate of the disease was presented as the ratio of the number of patients and the whole population according to the census as the denominator for 100,000 inhabitants.

More than two linked cases of the disease were considered as a potential epidemic.

Microbiological investigation

In the Centre for Microbiology of the IPH, the cases of the disease were confirmed by serology tests: SAT (standard agglutination test) Wright or BMAT (*Brucella micro agglutination test*).

According to the Ordinance on establishing measures for the early detection, diagnosis, prevention and suppression of spread, as well as eradication of infectious diseases of cattle, the method of implementation, and the manner of determining the status of farms free of brucellosis in all cattle, sheep, goats and pigs, all animals which were tested positive on brucellosis were stamped out. Laboratory diagnosis of brucellosis during this period was carried out by the methods of the Rose Bengal test, complement fixation, indirect ELI-SA and complement ELISA test as a confirmatory test. All samples were examined during the regular annual review and animal health protection monitoring was applied as ordered by the program of measures for each year on the territory of the Republic of Serbia. Samples of animals from all the registered farms as well as of animals in private ownership were taken. All animal samples were tested in the Scientific Veterinary Institute, Novi Sad.

The data were analyzed chronologically, demographically and topographically for the observed period by descriptive epidemiological study. We used the basic statistical indicators, general and specific incidence rates.

Results

In the observed period in Vojvodina, 102 cases of brucellosis were registered. The highest incidence rate of brucellosis was reached in 2004 when 35 cases of brucellosis with incidence rate of 1.8 cases per 100,000 populations (Figure 1) were registered.

Most patients in the territory of Vojvodina (80.4%; 82/102) were registered in the territory of the South Banat and the South Bačka District. The registered incidence rates were less than 0.2/100,000 inhabitants in the North Banat and the West Banat District. Cases of brucellosis were registered on the whole territory of the province (Figure 2) with exception of the North Bačka District.



Fig. 1 – Incidence rates and number of cases of brucellosis in Vojvodina, 2000–2014.



Fig. 2 – Incidence rate of brucellosis per 100,000 populations by districts in Vojvodina, 2000–2014.

Observed by modes of brucellosis transmission in the Province, distribution of brucellosis in two districts (South Bačka and South Banat) showed larger differences. On the territory of the South Bačka District the majority of 22 cases registered, which reached 68% of the patients, the spread of infection was caused by consuming dairy products homemade, purchased at city markets. On the territory of the South Banat Districts, out of 59 registered cases, food was pointed out by 19% of affected individuals as a possible way of spreading the disease. Most of the patients from the territory of the South Banat Districts (45% of patients) were professionally exposed to direct contact with animals, and 31% of the patients faced an alimentary risk by being with animals.

Out of the total number of patients (44 patients), 43.1% indicated daily direct contact with domestic animals in the maximum incubation period as the only possible way of spreading the infection. The consumption of thermally untreated domestic dairy products was represented in 27.5% of patients. Both possible modes of transmission were indicated in 22 patients (21.6%), whereas for 8 patients (7.8%), the mode of spreading infection remained unknown (Table 1).

In 74% of the cases, the sheep cheese was recognized as the food from domestic production which exposed patients consumed in the maximum incubation period. Cow's milk, cheese and raw milk was specified in 10–16% of patients as potential sources of infection.

Table 1

Probably modes of brucellosis transmission in Vojvodina by districts, 2000–2014.									
Mode of transmission	South Bačka	Srem	West Bačka	North Bačka	Central Banat	North Banat	South Banat		
wode of transmission	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		
Contact	3 (14.0)	5 (45.0)	0 (-)	0 (-)	8 (100.0)	1 (100.0)	27 (45.0)		
Incriminated food	15 (68.0)	2 (18.0)	0 (-)	0 (-)	0 (-)	0 (-)	11 (18.6)		
Contact and food	1 (0.9)	3 (27.0)	0 (-)	0 (-)	0 (-)	0 (-)	18 (31.0)		
Unknown	3 (2.9)	1 (9.0)	1 (100.0)	0 (-)	0 (-)	0 (-)	3 (5.0)		
Total	22 (100.0)	11 (100.0)	1 (100.0)	0 (0)	8 (100.0)	1 (100.0)	59 (100.0)		

Probably modes of brucellosis transmission in Vojvodina by districts, 2000–2014.

n – number of human brucellosis cases.

Data concerning the occupation of patients were defined for 94 patients. Occupational exposures to the agent or direct daily contact with animals were determined in 70.2% (66/94) persons. Infection among males was about three times more often registered than among females. The most common occupation appeared to be agriculturist, and there was 34.9% registered cases (Table 2).

In the observed period for the Province territory, 73% (74/102) of brucellosis cases were covered in 14 epidemic outbreaks of brucellosis. During 10 epidemic outbreaks of

the infection spread, 57 people were infected by direct contact with diseased animals. The alimentary mode of transmission was present in 4 outbreaks when 17 patients were infected, while individual cases of the disease were registered in 28 infected individuals (Table 3).

The largest number of patients (50%) belonged to the working age category of population (30–59 years). Registered 7.7% of infected patients were up to 19 years old. Males were 2.5 times more affected than females (Figure 3).

Half of the total number of the infected patients were

Table 2

Occupation and sex distribution	Male $(n = 49)$	Female $(n = 17)$	Total $(n = 66)$
Occupation	n (%)	n (%)	n (%)
Agriculturist	20 (40.8)	3 (17.6)	23 (34.9)
Rearer	11 (22.4)	1 (5.9)	12 (18.2)
Housewife	0 (-)	11 (64.7)	11 (16.7)
Veterinary Institute professionals	6 (12.2)	1 (5.9)	7 (10.6)
Cattleman	3 (6.1)	0 (-)	3 (4.5)
Stockbreeder	2 (4.1)	0 (-)	2 (3.0)
Agricultural cooperatives workers	1 (2.2)	0 (-)	1 (1.5)
Miscellaneous (student, painter, locksmith, unemployed, senior)	6 (12.2)	1 (5.9)	7 (10.6)

	Table 3
odina.	2000-2014.

Reported brucellosis case in outbreaks by modes of transmission in Vojvodina, 2000–2014.								
Mode of transmission	Number of outbreaks (n)	Number (%) of cases						
Direct contact	10	57 (77.0)						
Others modes	4	17 (23.0)						
Total	14	74 (100.0)						





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registered in the period from April to June. The smallest number of infected patients (5.8%) were registered in the period from October to December (Figure 4).

The epizootic characteristics of brucellosis in the South Backa District

In the period from 2001 to 2014, in the Centre for microbiology IPH 993 sera of patients from the South Bačka District, were tested and the disease was confirmed in 33 (3.3%) cases.

The highest percentage of positive results (91%) was recorded in 2004 and 2005, when the highest number of the infected patients were registered in the territory of Vojvodina. The last laboratory-confirmed case of brucellosis in Vojvodina was recorded in 2011. However, yearly in the IPH laboratory processing, an average of 66 serum samples of patients were analyzed due to suspected differential diagnosis of brucellosis in the South Bačka District.

In order to timely detect infected animals and proceed with their elimination, regular checkups and inspections of cattle, sheep, pigs, horses and dogs, in the period from 2001 to 2014 in the South Bačka District were performed and a total of 1,487,225 serum samples were analyzed, out of which only 1,498 (0.1%) were positive for brucellosis. In the period from 2003 to 2007 seropositive reports were registered in different animal species. In 2004 and 2005, there were animals with clinical symptoms, as well as abortions in females. The highest number of positive findings for brucellosis from sera of sheep and goats, were up to 1,316. The positive findings were detected in the serum of 168 pigs (153 in 2014), 13 cows and one in a horse serum sample (Table 4).



Fig. 4 - Seasonal distribution of brucellosis in Vojvodina, 2000-2014.

Table 4

The number of serology tested and serology positive for brucesellosis humans and animals in the South Bačka District, 2001–2014.

South Dacka District, 2001–2014.												
Years	Cows		Sheep and goats		Pigs		Horses		Dogs		Humans	
	Т	Р	Т	Р	Т	Р	Т	Р	Т	Р	Т	Р
2001	26,730	0	786	0	1,1917	0	296	0	0	0	5	0
2002	34,408	0	1,194	0	1,1826	0	332	0	3	0	9	0
2003	34,331	0	50,233	293	8,740	0	48	0	0	0	1	0
2004	37,619	3	91,052	449	11,241	4	202	0	3	0	148	10
2005	31,236	9	90,056	549	8,369	11	226	1	2	0	215	20
2006	9,160	0	56,224	20	3,593	0	0	0	0	0	96	0
2007	54,902	0	64,230	5	4,863	0	24	0	6	0	94	0
2008	58,015	0	108,369	0	11,736	0	4	0	2	0	86	0
2009	40,389	0	49,286	0	10,993	0	1	0	19	0	89	2
2010	37,891	0	67,475	0	3,301	0	3	0	11	0	52	0
2011	42,954	0	74,762	0	4,708	0	3	0	30	0	50	1
2012	40,229	0	71,090	0	2,586	0	0	0	7	0	39	0
2013	38,631	1	68,737	0	1,934	0	12	0	80	0	53	0
2014	39,611	0	67,162	0	3,133	153 ^a	179	0	30	0	56	0
Total	526,106	13	860,656	1316	98,940	168	1,330	1	193	0	993	33

T – Tested; P – Serology positive; ^aEcologically reared animals were caught and tested that year.

Discussion

Brucellosis is a disease that is widespread throughout the world, especially in countries with developed livestock breeding. According to the World Health Organization (WHO), about 500,000 people in the world are affected annually, including 20,000 cases registered in Europe. With different frequency, the disease is registered both in Europe and in the United States of America (USA). High-risk areas are the Mediterranean countries (Portugal, Spain, southern part of France, Italy, Greece, Turkey and North Africa), South and Central America, Eastern Europe, Asia, Africa, the Caribbean and the Middle East ^{6,7}.

A new risk area for developing human brucellosis is the region of Central Asia due to the deterioration of the epidemiological situation in Syria⁷.

Epidemiological surveillance of brucellosis in Vojvodina has been implemented from 1954. By the year 1970, in Vojvodina, individual cases of the infection were registered – in total there were 40 registered patients. The highest incidence was registered in 1965 with the incidence rate of 0.9 per 100,000 inhabitants. In the period from 1971 to 1999, despite the unfavorable epidemiological situation in the region, on the territory of the Province, brucellosis was not registered and was considered to be eliminated in Vojvodina. After three decades without any registered cases, in 1999 in the South Banat District brucellosis was registered in three infected patients, and epidemiological research determined that the infection came from imported animals (sheep)¹.

In the period from 2004 to 2007 a large epizootic and epidemic of brucellosis in Bosnia and Herzegovina (B & H) were registered. In the same period on the territory of Vojvodina the highest number (35) of patients were recorded with the incidence rate of 1.8/100,000 population in 2004⁸.

The epidemiological situation in the region is similar to the situation in Vojvodina, except in Slovenia, where brucellosis has been eradicated. According to the data from epidemiological service of the Republic of Slovenia, in the period from 1948 to 2013, there were 93 cases of human brucellosis evidenced. From the mid-fifties, only imported cases of the infection in humans were reported; they traveled through the countries where brucellosis was still endemic ⁸.

In 2006, the incidence of the infection in Serbia was 0.1/100,000 inhabitants, which was lower than in the EU countries recorded that year (0.2/100,000), while in Vojvodina, because of the epidemic spread of brucellosis, the registered incidence was identical to the average incidence of human brucellosis in the European Union⁹.

On the territory of the European Union, during 2012, 328 confirmed cases of brucellosis in human population were registered (0.1/100,000), which was 2.4% less than in 2011. The highest number of reported cases was from the territory of Greece (1.1/100,000) and Portugal (0.4/100,000), while the incidence of the disease was the same in Sweden, Spain, Norway and Austria (0.1/100,000)^{10, 11}. Together with Bulgaria, Serbia recorded the lowest rate of brucellosis incidence in the Balkans¹². Differences in the distribution of brucellosis incidence among districts of the Province can be inter-

preted as the result of the exchange of livestock fund among these regions (e.g. South Bačka and South Banat) and in neighboring countries, especially B & H.

In relation to the seasonal distribution of the infection, in endemic countries the highest numbers of patients are registered in June and July ^{13–15}. On the territory of countries where the disease is not endemic, seasonality does not show variation in reporting. On the territory of Germany, the highest number of cases are usually reported in August and September, when German citizens, originally from Turkey, return from vacations and bring with them incriminating foods in the form of dairy products (unpasteurized goat cheese) originating from Turkey ¹⁶. In central Greece, where brucellosis is an occupational disease, most cases are reported during March and May ¹⁷.

The results of our study show that the greatest number of patients was registered in April and May. During these months the lambing and kidding sheep and goats are done, as well as intensive milking, sheep shearing and other activities in which humans are in contact with potentially infected animals.

In countries where preventive measures are carried out in order to prevent the spread of brucellosis through food, brucellosis is primarily an occupational disease and mostly affects male patients between 20 and 45 years of age. The incidence of infection in children is higher in countries where the common way of spreading infection is through thermally unprocessed food products of animal origin, which is typical for nomadic society ⁶.

The results of our investigation showed that half of the total number of patients belonged to the economically active population. The largest number of cases was reported in the age group of 30 to 59 years of age.

During the epidemic spread of brucellosis on the Greek island of Thasos in 2008, where 98 people were infected, alimentary mode of infection spreading was dominant and locally produced cheeses were labeled as incriminated foods¹⁸.

In the observed period, in Vojvodina, alimentary mode of transmission was detected in every fourth patient, with the largest number of patients infected after consumption of incriminated foods during outbreaks in South Bačka District, the City of Novi Sad. The largest number of infected patients in this part of the Province can be explained by the fact that Novi Sad is the largest city in the Province with a developed network of services in the form of market supply of milk and milk products from different parts of Vojvodina.

The different way of production process and the preparation of the cheese in domestic conditions may contribute to increasing concentrate of *Brucella* spp, which in this type of foods can last up to several months. Since the beginning of the 1990s it was well known that alimentary mode of transmitting is more important in cities, where the infection is registered among patients who consumed dairy products from the previously untreated milk from domestic production; these incriminating groceries were bought at city markets².

Frequent distribution of these types of food from endemic countries may jeopardize the process of elimination and eradication of the infection in the territories of developed countries. In Germany, human brucellosis was registered as an occupational infection, but by entering different incriminating store, brucellosis is still registered in the general population ¹⁶.

In the area of Vojvodina sheep cheese was registered as the most common food that provokes the infection in individuals. It is known that milk products of sheep and goats *B*. *melitensis* bring higher risk to individuals who would not otherwise be professionally exposed to these animals, but they consume their meat and milk ^{19, 20}.

In our study, the contact mode of infection spreading, as the only possible route of the infection transmission, was registered among 43.1% of the registered cases. Observed by districts of the province, this contact mode of transmission was usually detected in the South Banat District, where a total of 59 patients were registered with known epidemiological data, while 46% of patient's data on contact with the animals were obtained.

Number of epidemic contact in the Province is higher in relation to the rest of the Republic of Serbia. This is explained by the existence of a more developed sector of animal husbandry and greater opportunities of exposure to potentially infected animals ¹². During the observed period, out of 74 patients, 57 affected individuals, had a direct in contact with diseased animals, while 17 patients were registered in the outbreaks with alimentary modes of transmission.

Gender-specific distribution of the infection is different from country to country. In Greece, brucellosis is an occupational disease and is diagnosed three times more in males ^{18, 21}.

In the area of Germany after 2000, there were no gender-specific differences (54% male: 46% female), ¹⁶ unlike Uganda where the majority of infected patients were females, who were in daily contact with animals ²².

In our study, 70% of the affected people (farmers, workers flocks, workers in the Veterinary Institute, homemakers on farms, shepherds and cattle breeders) had occupational exposure to animals. In relation to gender specificity, men were 2.5 times more likely to be infected in comparison to females. These data can be explained by the fact that professional exposure and exposure in households are more characteristic for men than women.

In support to the favorable, declining trend of brucellosis in Vojvodina, goes the fact that over the past five years only one case of human brucellosis was detected, and that in the last 9 years no outbreaks of brucellosis in Vojvodina were registered. This favorable epidemiological situation is also the result of previously taken measures to remove the animals that were positive for brucellosis.

Besides on the territory of the Province, from 2005 the declining trend of the brucellosis incidence was also registered in the territory of the South Bačka District, both in humans and animals. During 2014, brucellosis was detected in pigs that represented a population of domestic animals who lived in the pasture released (i.e. an environmentally friendly way of growing animals). These pig populations are often in contact with wild reservoirs of brucellosis infection. This method of raising animals complicates monitoring and implementation of diagnostic procedures, as well as regular annual sampling.

In recent decades, in the EU countries, various programs were implemented for cattle, sheep, goats and pigs to control, suppress, eliminate and eradicate brucellosis with disputable success. The brucellosis incidence in animals varies among different countries of Europe, and in some cases, there are variations among different regions of the same country. North European countries have the status free of brucellosis in cattle (*Brucella abortus*), sheep and goat brucellosis (*Brucella melitensis*). In the countries of Southern Europe, the brucellosis incidence in animals, particularly in sheep and goats, is similar to that in humans, where there are still registered cases of infection with *B. melitensis*. As a result of contact with wild pigs, cases of brucellosis occasionally registered are among pigs that are pasture released (*Brucella suis* biovar 2)²³.

Conclusion

Data from the IPH of Vojvodina on the number of tested people on the territory of the South Bačka District indicate the continuity in the number of people who were being tested, which is in favor of prudence in the differential diagnosis of patients with atypical clinical course suspected of brucellosis.

Due to the long incubation period and nonspecific clinical presentation of the disease, the restrictions in establishing the definitive diagnosis of brucellosis are evident, and for the majority of patients it is not possible to determine the infection reservoir.

Although the incidence of brucellosis shows a declining trend, education and improving of surveillance of disease by all relevant institutions seems to be necessary for better recognition and notification of the disease.

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