

## RESPIRATORY DISORDERS OF FARMED RABBITS: OCCURRENCE AND RISK FACTORS

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**Abstract:** In this study, we focused on the occurrence of respiratory disorders in rabbit farms, as well as several risk factors. We based the assessment on 11 217 visits to 1288 commercial farms in Spain and Portugal from 1996 to 2020. There was a sub-set of 307 visits due to respiratory system issues on 172 farms; the main causes were high prevalence of rhinitis in does and high mortality risk in weaned rabbits. During the 25-yr observational study, we physically examined 29 000 males and 200 000 lactating does to monitor their sanitary status on 894 farms. The mean annual prevalence of clinical rhinitis (CR) and 95% binomial confidence interval (CI) in does was 19.9% (95% CI [19.7-20.1%]). We observed an improvement as prevalence of annual CR fell from 29.6% in 1996 to 15.2% in 2020. The main risk factor for rhinitis was the rabbit line, followed by gender (males become sick more than females) and age of females. The median age of farmed does was 5 parities (minimum to maximum: 1-39). The enabling risk factors were year, season (more often affected in summer) and service timing (lowest prevalence when does were served  $\geq 32$  d postpartum). In a sub-set of 208 farms, we determined the prevalence of apparent atrophic rhinitis, which was 0.04% in females and 0.11% in males. Concerning bacteriological studies with 444 samples from 153 farms, *Pasteurella multocida* and *Staphylococcus aureus* were the main agents isolated from cases of pneumonia, rhinitis and other issues. We may infer that much work is required to determine in greater detail the factors linked to the farm environment and apply this knowledge in practice.

**Key Words:** rabbit, respiratory diseases, rhinitis prevalence, animal welfare, disease prevention.

## INTRODUCTION

Respiratory diseases of rabbits include a) rhinitis and other issues related to the so-called respiratory syndrome (Flatt, 1974), such as respiratory distress, head tilt, dull eyes, poor body condition and lesions: external otitis, subcutaneous abscesses in the abdominal region or throat (Coudert *et al.*, 2006). There is also b) pneumonia in adults, kits or weaned rabbits (Lund, 1951). In a previous study in Spain, respiratory diseases accounted for 7.2% of urgent farm visits, the second cause after 49% due to digestive diseases (Rosell *et al.*, 2009). During 1983-1985, the prevalence of rhinitis assessed in 101 doe farms was 41% (Badiola *et al.*, 2000). Morisse *et al.* (1984) found 27-54% affected

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does in 26 French rabbitries. More recently, prevalence was 25 and 30% in farmed females and males, respectively (Rosell, 2003). Rabbits with severe respiratory disorders show a drop in productivity and display signs of pain, affecting their welfare (Broom and Fraser, 2015). In fact, airway diseases are life threatening; pneumonia (including pleuritis) caused 0.7% and 0.9% monthly mortality risks in adult females and males, respectively (Rosell and de la Fuente, 2016).

Health monitoring of farmed rabbits includes checking for rhinitis (Morisse *et al.*, 1984); this disease often produces secretions and is also known as *snuffles*, *contagious nasal catarrh* (Hoskins, 1920) or *contagious coryza* (Löfger *et al.*, 1972). Snuffles cases in rabbits >6 wk old are chronic and very often irreversible (Cowie-Whitney, 1977). Signs of rhinosinusitis frequently include sneezing; rabbits do not cough. Severe rhinitis can affect the general condition of the animal. Besides, given the close connections with several organs (Johnson-Delaney and Orosz, 2011), an infection of the upper respiratory tract can lead to other disorders, e.g. in lungs, ocular conjunctiva, ears, genitals, and even septicaemia (Kpodékon, 1983). The diagnosis of clinical rhinitis is based on observing nasal, mucosal, purulent and sometimes scabby secretions in the nostrils, on the medial surface of the forelimbs, or both (Webster, 1924). Airway diseases can have various causes; however, our study concerns on-farm clinical infections. *Pasteurella* spp., and mainly *P. multocida* are key agents in rabbit medicine; they are opportunistic or primary pathogens (Christensen *et al.*, 2014). *Staphylococcus* spp., mostly *S. aureus*, cause several disorders including respiratory issues (Corpa *et al.*, 2009). There are high- and low-virulence strains that can induce either severe or mild problems, respectively (Haag *et al.*, 2019).

The epidemiology of respiratory diseases in farmed rabbits has similar traits as in other production animals; e.g., outbreaks are likely multifactorial (Constable *et al.*, 2017). There are predisposing risk factors such the age of the host (Hagen, 1958; Holmes, 1988). Concerning gender, in a previous study we found higher prevalence of clinical rhinitis (CR) in males than in does. Moreover, there are enabling risk factors of disease, such as season and husbandry. Rabbit housing should be mentioned as a main source of aggressions; it includes *static* elements, such as the promiscuity of adults and weaned rabbits in the same barn, and *dynamic* elements, such as temperature, wind speed, noxious gases, dust or airborne bacteria (Rosell *et al.*, 1992). Public Health is a main goal in respiratory issues related with rabbit production, as their agents are potentially zoonotic (Ekstrand and Woodford, 2021); antimicrobial reduction is also a priority (EFSA, 2021). Respiratory diseases cause economic damage due to death, decreased fertility, lower average daily gain or feed efficiency and the cost of disease control (Cartuche *et al.*, 2014). Moreover, producers cull rabbits unfit for consumption (e.g., with subcutaneous abscesses, related with pasteurellosis), and there are abattoir condemnations (Ferreira *et al.*, 2014). Lastly, these diseases and their control have been the subject of research and continuous education worldwide (Webster, 1924; Ostler, 1961; Rossi, 1976; Coudert *et al.*, 2006; Cervantes *et al.*, 2019; Wang *et al.*, 2020, among others).

Our aims were to (1) describe clinical visits due to respiratory diseases on rabbit farms between 1996 and 2020; (2) determine the prevalence of CR, including the atrophic form, in breeding rabbits; (3) investigate predisposing risk factors for rhinitis, such as gender, rabbit line, age and intercurrent diseases (e.g., mastitis); and (4) estimate the enabling risk factors of rhinitis, such as seasonal effect and breeding practices.

## MATERIAL AND METHODS

Our 25-yr study lasted from 1st January 1996 to 31st December 2020. We gathered the retrospective information by analysing the records of 11 217 visits, as part of daily veterinary practice, routine health monitoring and surveillance, and consulting activities on farms housing females, males or weaned rabbits in Spain and Portugal. Animal Care and Use Committee approval was not needed for this study, as the data were obtained from rabbits raised under commercial conditions; farms fulfilled European, national and regional recommendations and laws on animal welfare, food safety and environmental protection.

### *Characteristics of the farms being visited*

The present observational study includes the visits made by the first author to 1288 farms; 1214 in Spain and 74 in Portugal. They were mainly breeding-finishing farms, with a continuous flow of young females through breeding barns

(10% monthly). Taking into account that in July 2017 there were 906 and 139 rabbit farms housing >20 females in Spain and in Portugal, respectively, the visited farms represent a main proportion of the farms present in the Iberian peninsula (Rosell and de la Fuente, 2018). The farms had different *habitat* characteristics, e.g. open-air or indoor farms, space and air volume per rabbit and manure system; all rabbit does were single-housed and 87% had footrests. There were several *environment* traits, in particular temperature, relative humidity and air speed. The respiratory system is greatly influenced by these variables, in addition to the air flow and concentration of dust and gases, mainly ammonia. Microclimate observation and control was included in the protocol of most visits, whenever possible objectively measured, e.g. with data loggers (Calvet *et al.*, 2012). The number of yearly visited farms and sizes are reported in Table 1, in Rosell *et al.* (2020). On each visit, we asked producers about their rabbit breeds and lines, doe inventories, i.e., females bred once or more, generally at 4.5-5.5 mo old. In Spain and Portugal, the majority of food-producing rabbits are commercial breeding lines, with the exception of New Zealand White rabbits, and non-selected “coloured” rabbits (de la Fuente and Rosell, 2012).

### ***On-farm management procedures***

We visited open-air and indoor farms, with natural or mechanical ventilation; images may be seen on our website (Rosell, 2020). We recorded the breeding practices used on each farm, e.g. the type of service, i.e., if does were bred by artificial insemination (AI) or naturally mated, and the AI centre supplying semen, if any. In addition, we noted the service timing; rabbit farmers use a fixed service time from 11 to 60 d after parturition. We also recorded the number of batches per farm, from 1 to 8; a batch is a group of rabbit does serviced on the same day. The use of a single batch allows the “all in-all out” system to be used and housing to be cleaned and disinfected (Huneau-Salaün *et al.*, 2015). A farm could have, for example, 1000 does in 2 batches; one with 400 at the point of parturition and another with 400 lactating does, 40-50 of which we examined. In addition, there could be 200 empty or pregnant non-lactating does.

### ***Veterinary visits to the rabbit farms***

In this study, the clinical information on productive and sanitary events was collected during veterinary visits of the first author to the rabbit farms, from January 1996 through December 2020. It should be taken into account that data were gathered during the visits to farms and did not follow an optimally balanced design. A key aspect in our practice is that often the visits were conducted regularly in the farms at the initiative of the attending veterinarians; others were at the request of the producers. When classifying the visit, we only considered the main cause, e.g. check-up (no relevant problems) or diseases such as respiratory or myxomatosis, amongst others (Rosell, 2003). We also asked the farm staff questions about procedures for disease prevention: for instance, biosecurity practices, vaccination schedule and metaphylactic treatments. In a previous article (Rosell *et al.*, 2019), we showed a geographical distribution of visited farms and yearly or monthly distribution of farm visits. To check for possible confounding, it was not opportune to examine the animals in several visits; e.g., when diseased females had been culled from a batch. Besides, we avoided checking females when they were around the service or kindlings, or in visits due to severe processes of the digestive system or RHD (rabbit haemorrhagic disease). Lastly, in the visits for myxomatosis we did not check for rhinitis in breeding rabbits either. Accordingly, this could have caused an underestimation of the prevalence of rhinitis, since myxomatosis viruses are immunosuppressive and allow bacterial infections (Marlier *et al.* 2000).

**Table 1:** Characteristics of the databases gathered from 1996 until 2020 and used for the present study.

Database	Traits	Record N	Cohort N	Farm N	Period
1	Visits for respiratory disorders	307	NA	172	1996-2020
2	Examinations of does by farm	200 843 does*	4 003	894	1996-2020
3	Individual examination of does	50 230 does*	854	265	2006-2020
4	Examinations of males by farm	29 050 males	1 821	540	1996-2020
5	Assessment of atrophic rhinitis by farm	37 396 does*, 22 247 males	1 265	208	2001-2020
6	Microbiological analyses	442	NA	152	2001-2020

\* Lactating females. NA: not applicable.

### Sampling protocol

The protocol for on-farm monitoring and surveillance of CR included the examination of a sample of males or females; we targeted only lactating does. Sample size ( $n$ ) was calculated using *WinEpi* software (De Blas, 2006) considering the population at risk (*by groups of animals*), expected confidence (95%) and expected prevalence ( $p$  %). Concerning females, e.g. with a known  $n$  of does to be examined in each cohort, as a first step, we checked 10 to 15% of primiparous does, which corresponded to the mean percentages of new does per batch (Coutelet, 2015). Then, we proceeded with the multiparous does using random systematic sampling; e.g., if  $n=60$  and we examined 8 primiparous dams in a cohort with 550 at-risk females, for the remaining 52 we examined 1 doe from every 10. In some cases, farms were sampled in 2 consecutive months; therefore, a keeping track procedure was applied to avoid repetitions of does. These morbidity assessments were supported by the exploration of does outside their housing. In lactating females, we checked for the presence or not of CR, mastitis, ulcerative pododermatitis and mange, following the protocol previously described (Rosell, 2003). All these criteria were classified as binary variables. The case definition of a rabbit affected by CR was based on Webster's description (Webster, 1924). The body condition score (BCS) was assessed using a linear scale from BCS=1 (emaciated) to BCS=9 (obese), with BCS=5 as the optimum (Sánchez *et al.*, 2012). In our monitoring study, there might reasonably have been different omissions and biases. Our results are mainly based on clinical examinations only, and despite the use of a defined protocol, some incorrect diagnoses are possible.

### Diagnostic procedures used

Diagnostic approaches for respiratory status mainly included the clinical signs and gross pathological postmortem findings at on-farm necropsies. Flatt and Dungworth (1971) revealed the existence of on-farm silent pneumonia, detected at slaughter. Thus, we complemented several preliminary diagnoses with observations at slaughter, personally in the abattoir work chain, also with information from inspectors or academic centres (Vidal *et al.*, 2016) and by laboratory follow-up. We diagnosed on-farm *respiratory illness* when (a) we did not detect any more serious problems, for example myxomatosis, RHD or severe digestive processes, among others; (b) when pneumonia or haemorrhagic septicaemia were the main causes of death (Figure 1); (c) when threshold values for the prevalence of rhinitis were: >25% of lactating females and >30% of adult males or an increase compared to previous visits to the



Figure 1: Rhinitis can be severe *per se* and predispose to infections in other organs, such as the lungs.



Figure 2: We analysed cases of otitis externa, caused mainly by *Pasteurella multocida*.

farm (case definition of affected cohort or farm); farms without problems should have <15-20% of rabbits affected. Lastly, (d) *in vivo* directly listening for rabbits sneezing, or by visual observations of other clinical signs: dyspnoea, torticollis and gross lesions: otitis externa (Figure 2), or ventral or throat subcutaneous abscesses by palpation, also afforded a positive diagnosis.

We made the clinical diagnosis of atrophic rhinitis when we saw deformation of the snout profile (Figure 3).

### Laboratory procedures

*Pathology laboratory:* live rabbits, for example with atrophic rhinitis, or organs (mainly lungs, heart, ears and uterus) collected in the on-farm necropsies and fixed in 10% buffered formaldehyde for 48 h, were sent to the laboratory for histopathologic study. Samples were routinely processed, stained with haematoxylin and eosin (HE) and Gram staining.

*Microbiology laboratory:* a nasal swab or a fragment of tissue, e.g., lung, kept at room temperature for short periods, was sent to the lab. For longer periods, the samples were frozen. For the isolation of *Pasteurella multocida* and *Staphylococcus aureus*, we used Columbia Agar with 5% sheep blood (CA, bioMérieux). The plates were incubated at 37°C for 24h in aerobiosis and the colonies obtained were then observed. Once we isolated the CA colonies, we reseeded each of the strains on another CA plate and incubated them again for 24h at 37°C in aerobiosis. Suspect strains were run through bioMérieux's Vitek-2 system with GN (for *Pasteurella*) and GP (for *Staphylococcus*) cards for identification. *Bordetella* strains were not searched for, but in some cases they were abundant in the plates and were therefore identified. The same thing occurred with *Streptococcus* spp.

### Data recording

For the present observational study, we distributed the information in 6 databases (Table 1). Information was recorded in the farm in paper form and then compiled on different spreadsheets.



Figure 3: Atrophic rhinitis. Other related images may be seen in Rosell (2022).

The 1st database refers to visits made due to a clinical problem. Databases 2, 4 and 5 refer to disease occurrence determined by evaluating farm-level. Database 3 includes disease occurrence by animal-level prevalence (Hoinville *et al.*, 2013). Some databases are recorded by cohorts: batch subgroups including a set of females served on the same day in a maternity barn or on a farm, which have another trait in common, e.g., physiological condition or rabbit line.

### Statistical analysis

When the examination was performed, we calculated apparent prevalence of CR with the population of breeding rabbits at risk (lactating does, males), sample of examined rabbits ( $ne$ ), sick rabbits found ( $ns$ ), and expected degree of confidence (95%). We converted our anonymised raw data to Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA). Statistical analysis was performed by SAS Institute (2004) (Statistical Analysis System, version 9.1) utilising GLM, GENMOD and FREQ procedures, according to the statistical model. Statistical significance was declared by a  $P$ -value  $<0.05$ . The dependent variable: *prevalence of CR* was binomial (proportion) distribution in the GLM procedure with a logit link function. The units of analysis were the 4003 (females) and 1821 (males) cohorts, (proportion:  $ns$  sick rabbits /  $ne$  examined rabbits). The factors of variation on the dependent variable: CR prevalence were estimated with the following model:  $Y_{ijkm} = \mu + A_i + S_j + YS_{ij} + L_k + R_l + e_{ijkm}$ , where  $Y_{ijkm}$  was the dependent variable: *prevalence of CR* on each farm visit,  $\mu$  was the mean,  $A_i$  was explained by the effect of the  $i^{\text{th}}$  year (25 levels),  $S_j$  was explained by the effect of the  $j^{\text{th}}$  season (4 levels),  $L_k$  was explained by the effect of the  $k^{\text{th}}$  rabbit line (16 levels);  $R_l$ , the effect of the  $l^{\text{th}}$  service timing (4 levels: 11, 18, 25,  $\geq 32$  d after kindling), and  $e_{ijkm}$  was the *residual effect*.

With regard to the dataset with 50 230 records (does), we used the GENMOD procedure with a logit link function to analyse *individual rhinitis* as binomial (+ vs. -), with the model:  $Y_{ijklmn} = \mu + R_l + S_j + K_k + BC_p + H_m + e_{ijklmn}$ , where  $Y_{ijklmn}$  was the dependent variable, *rhinitis on each checked female*,  $\mu$  was the mean,  $R_l$ , the effect of the  $l^{\text{th}}$  service timing (4 levels: 11, 18, 25,  $\geq 32$  d after kindling),  $S_j$  was explained by the effect of the  $j^{\text{th}}$  season (4 levels),  $K_k$ , by the effect of the  $k^{\text{th}}$  number of kindling (9: 1 to 8, and  $>9$ );  $BC_p$ , the effect of  $l^{\text{th}}$  BCS (7: 2 to 8);  $H_m$ , the effect of the  $m$  sanitary status (3: mastitis, sore hocks, mange); and  $e_{ijklmn}$  the *residual effect*. We present the prevalence of CR with the 95% binomial CI.

## RESULTS AND DISCUSSION

### Visits related to respiratory diseases

From January 1996 until December 2020, we made 307 visits due to airway diseases on 172 farms; they were much less frequent than visits due to digestive diseases (1841). The most common issues were high prevalence of rhinitis in breeding rabbits, followed by high mortality risk in growers and adults. In Table 2 there are new cases, without repeated disease detections.

More specifically, we include the following clinical cases diagnosed in the last years of the study period, caused by *P. multocida* (identified) and 1) producing pneumonia and even haemorrhagic septicaemia (HS) in 1st parity does. We highlight the proportional study of Seidel (1936), with 10 000 necropsied rabbits, and HS causing death in 1249 cases. We observed 2) 10% mortality from pneumonia in kits aged 21-35 d old, compatible with poor hygiene of nests. Care of kits is an essential task in rabbit production (Combes *et al.*, 2018), as well as the rearing of young does (Martínez-Paredes *et al.*, 2018), or 3) weaned rabbits with enzootic pneumonia, affecting their growth, causing 20% mortality from 55 d old onwards, increasing runts and condemnations at slaughter; e.g. for abscesses, as pointed out by Conficoni *et al.* (2020) (Figure 4). In addition, 4) there was a farm with otitis externa in weaned rabbits in summer and 5) one case with 2% of 57-d-old growers with atrophic rhinitis, compatible with very poor air quality. In cases of acute evolution (Figure 5), it was necessary to complement the diagnosis with rapid on-farm tests or laboratory follow-up.

### Prevalence of rhinitis in farmed lactating does

In the course of the 25-year study we gathered information on 4003 cohorts during 3600 visits to 894 farms, and included 200 843 examined lactating does. The mean size was 50.2 examined does over 422 does at risk per cohort.

**Table 2:** Main reasons for 307 visits on 172 farms due to respiratory events from 1996 to 2020.

Type of visits for respiratory disorders	N	%
High prevalence of rhinitis in lactating females, in males or both	133	43.3
High mortality risk and necropsies of weaned rabbits	49	16.0
High prevalence of rhinitis in weaned rabbits	35	11.4
High mortality risk and necropsies of breeding rabbits	25	8.1
On-farm diagnoses of subcutaneous abscesses in weaned rabbits	13	4.2
Poor sanitary status of breeding rabbits, including rhinitis	11	3.6
Relative increase in prevalence in relation to previous examinations	10	3.2
Visits to abattoirs due to high condemnations	9	2.9
Visits due to treatments related with respiratory conditions	8	2.7
High mortality risk and necropsies of kits (< 35 d old)	7	2.3
Visits with special attention to otitis externa in does or weaned rabbits	4	1.3
Visits with special attention to atrophic rhinitis (adults, weaned rabbits)	3	1.0

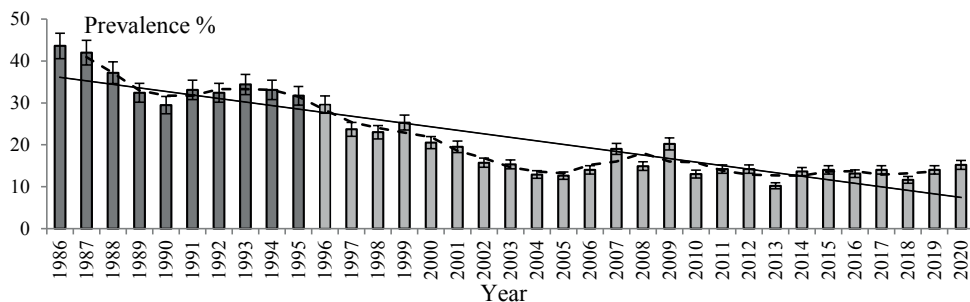
The mean annual prevalence of CR in does was 19.9% (Confidence Interval 95%:19.7-20.1%), ranging between 0% prevalence of CR and 95% (farms with persistent clinical signs). At the beginning of the period, prevalence was 29.6%, decreasing to 19% in 2007 and reaching 15.2% in 2020. The most recent outcome may be a baseline threshold when assessing sanitary status of farmed does, and the interference level: >25% CR. Figure 6 shows the prevalence data from the current study, comparing the results from a previous study performed in the same farms with prevalence of CR from 43.6% in 1986 to 31.7% in 1995 (Badiola *et al.*, 2000).



**Figure 4:** Abscesses are main causes of condemnation in abattoirs.



**Figure 5:** A 50-d-old rabbit died with an acute condition. It was compatible with various causes. The field test was negative for RHD. In the laboratory, *Streptococcus* spp. was isolated from lung.



**Figure 6:** Mean relative and annual prevalence of rhinitis of lactating does, and SEM, rolling average for three years (dotted line) and trend. This study was based on the clinical examination of 93 069 does in 3013 cohorts and 691 farms (darker columns), from 1986 until 1995 (Badiola *et al.*, 2000), and 200 843 does from 1996 onwards in 4003 cohorts and 894 farms (present study).

We consider that this improvement in the course of 35 yr was not due to changes in our work protocol, but to progress in a variety of factors, mainly due to the greater specialisation of rabbit producers. The models used in the statistical analysis have some limitations when applied in observational studies, but these limitations might be compensated by the large registered population sizes of rabbits individually examined. We believe that this article reflects the evolution of the Iberian rabbit farms in the course of this 25-yr study, in terms of kinds and sizes of farms (mean was 473 does in 1996 and 800 does in 2020), and food, rabbit lines and reproductive management. From an overall perspective, *Pasteurella multocida* can be present in almost 100% of conventional-rabbits >5 mo old (Nakagawa *et al.*, 1986), colonising the upper respiratory tract as a commensal or opportunistic pathogen. *P. multocida* might cause morbidity, depending on the reciprocal actions between the host's immune system, the healthy airway microbiota and the risk factors (Mach *et al.*, 2021). In commercial farms, there are examples such as environment of newborn and kits in the nests, weaning stress, overcrowding, aerosol transmission and infection pressure (Coudert *et al.*, 2006), as well as some vaccinations against myxomatosis or antimicrobial misuse; likewise, the cold air stream: e.g., >0.1 m/s. at 15°C, noxious gases: e.g., >10 ppm of ammonia or abrupt changes in temperature: >6°C/hour (J.S. Ferré, personal communication).

### **Prevalence of rhinitis in females and on-farm risk factors**

The second database included rhinitis prevalence results by farm, as shown in Table 3; the model was significant ( $P < 0.0001$ ),  $r^2$  value 0.43.

The five factors analysed were significant. The leading variable was *the line of breeding rabbits* (16 recorded rabbit lines or genetic types). The most affected line during the 25 yr had 48.7% rhinitis. In contrast, the rabbit line least affected had 12.2%. Coudert and Brun (1986) found different morbidity risks of coryza, among other disorders, in females of 4 rabbit lines. Moreover, with this evidence we understand efforts made to enhance the *resistance* of

**Table 3:** The General Linear Model of the risk factors *year*, *season*, *day of service* and *line of the doe* for the *prevalence of clinical rhinitis*, based on physical examination of 200 843 does in 894 commercial rabbit farms in Spain and Portugal, between 1996 and 2020.

Factor of variation	df	F-Value	$p > F$
Year	24	31.42	<0.0001
Season	3	35.14	<0.0001
Year×Season	72	2.96	<0.0001
Day of service	3	37.03	<0.0001
Genetic type of the doe	15	129.04	<0.0001



rabbits to pasteurellosis, among other diseases (Garreau *et al.*, 2021). Another concept of interest is *robustness*, which is related to rabbit size and allocation of nutrients, according to Pascual *et al.* (2013). Besides, the genetic background might partially determine *disease resilience* (Friggens *et al.*, 2022) and probably influences the rabbit immunocompetence (Mage and Rogel-Gaillard, 2021).

Differences between year and season were significant. There were more affected does in summer (19.4%) and fewer in autumn (14.5%); spring and winter were transition periods (17.4 and 14.8%, respectively). This climatic effect is consistent with previous findings. It is not clear why this seasonal effect exists in our latitude, but it has been hypothesised that two clusters of risk factors—high temperature and relative humidity or cold and draught—might cause climatic stress (Rosell *et al.*, 1992, 2009). Morisse (1981) showed the importance of adequate static volume: 2.5-3 m<sup>3</sup> per doe, to regulate air speed efficiently. In agreement also with the findings of Kawamoto *et al.* (1990), there is a relationship between environmental parameters and the prevalence of rhinitis, and even with the rabbit producer's health. In addition, abattoir condemnations due to subcutaneous abscesses of adults and young rabbits are higher in summer (Conficoni *et al.*, 2020). Lastly, farm staff should approach the control of the environment as an ongoing process, preventing it from becoming a risk. Nevertheless, more studies are needed in these core aspects (Calvet *et al.*, 2012). Assessment of airway disorders and measurement of environmental variables might be an interesting target for precision livestock farming surveys.

In database 2, with 894 farms, we analysed breeding practices. The type of service (mating or insemination) had no effect on the prevalence of rhinitis; there were 1291 cohorts with mating at 11 d after kindling, and 21.5% of prevalence of CR. In 1816 cohorts with AI at 11 d, prevalence was also 21.5%. Concerning service timing, the effect of this factor was significant. The risk of onset of CR has a clear decrease in farms with a longer kindling-to-kindling interval; the results are shown in Table 4.

The increase in the kindling-service interval might be another positive reason for the lower occurrence of rhinitis. In 1997, in 66 of over 212 farms being visited, rabbit does were rebred 1 to 7 d after kindling; in 2019 none used this service timing (Rosell *et al.*, 2020). However, on farms where does are served  $\geq 32$  days after kindling, young rabbits are even sold while still with the mother at 65 d; and they take feed and milk, since lactation ends 30 d after conception Lebas (2021). In agreement with Savietto *et al.* (2016), there was probably a lesser effect of production on the immune system. Does serviced  $\geq 32$  d after kindling cope with environment variables (Broom and Fraser, 2015), and which also affect fertility, as pointed out in a previous survey (Rosell *et al.*, 2020). This outcome is more compatible with non-resilience factors (Friggens *et al.*, 2022).

### **Individual study of rhinitis prevalence in females**

The 3rd database included 50 230 checked lactating does, individually recorded to determine their sanitary status and body condition. The significant factors of variation were season, service timing, number of kindling, BCS ( $P < 0.0001$  for the set of variables) and intercurrent diseases.

Figure 7 shows the age distribution of individual examined females. The sampled population was gathered on 854 cohorts (mean 58.8 does). Concerning the reproduction rhythm, 73.8% of the checked does were serviced at 11 d after kindling, 10.3% at 18 d, 11.3% at 25 d and 4.6% at  $\geq 32$  d; in France,  $>90\%$  used 11 d (Coutelet, 2015). The median kindling order was 5 (minimum to maximum 1-39 parities), and the mean was 6.1. This age pattern may be considered a reference, e.g., when monitoring lifespan (Friggens *et al.*, 2022). With regard to the BCS, the median was 4 and the mean 4.2. There was a close relationship between rhinitis and BCS: animals with values  $< 4$  present prevalence of CR=33.5% while prevalence decreases to 6.2% if BCS $> 6$ . Sick females had lower BCS as would be expected, in agreement with previous results (Sánchez *et al.*, 2012). We also measured the effect of age through kindling number, and it was significant. The distributions of prevalences are shown in Figure 8.

**Table 4:** The effect of the day of service after kindling on the prevalence of clinical rhinitis.

Service timing	11 d	18 d	25 d	$\geq 32$ d
Cohorts examined (N)	3017	414	309	173
Prevalence of rhinitis (%)	21.5	17.9	12.9	8.4

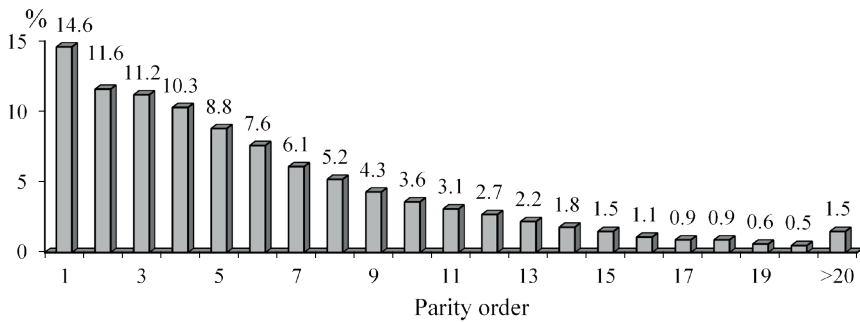


Figure 7: Descriptive age traits of female rabbits examined (n=50230) on 265 farms in Spain and Portugal, from 2006 to 2020.

The *age* of females was a predisposing risk factor for rhinitis. Prevalence showed an increase in the course of the three first kindlings and a decline after the 3rd parity. We believe that this misleading (false) effect is due to the risk of culling and mortality (Figure 8), including airway issues, which masks the true risk of rhinitis. In a previous study (Rosell *et al.*, 2020), 70% of producers used the 42-d cycle (AI at 11 d postpartum). The kindling-to-kindling interval per doe was 51.4 d from the 1st service of young does at 147 d, plus 31 d gestation. Thus, does with one parturition were 6 mo old; that is 12 parities per 2-yr-old female. Lastly, there was an effect of *intercurrent diseases* on rhinitis in females. When all the diseases were jointly considered, we observed 28.4% of sick animals. Mean prevalence of CR was 20.4%, prevalence of clinical mastitis was 4.2%, sore hocks: 5.8%, and mange was 2.5%. Mastitis had an effect ( $P=0.0071$ ) on prevalence of CR; does with both disorders had 23% prevalence while the prevalence of CR in animals without mastitis was 20%. This is logical, to the extent that there are common risk factors and microbial agents (Morisse, 1981).

### Prevalence of rhinitis in rabbit males

Database 4, with 1821 cohorts, showed a mean prevalence of 29.7% CR in males; during 25 yr it decreased from 44.7% in 1996 to 21% in 2020. Using the GLM procedure, the effects of *rabbit line*, *year* and *season* on the health of males were significant ( $P<0.0001$  for all the variables), similar to females (Table 3). The influence of the semen microbiota on doe reproductive tract is essential, as pointed out by Marco-Jiménez *et al.* (2020).

### Prevalence of rhinitis depending on gender

In a sub-set of the 2nd and 4th database there were 1358 cohorts with males and females on the same farm (n=510), excluding 30 large AI centres, since they do not have females. To perform this analysis, we included only farms with couples of the same rabbit line. Mean prevalences were 33% for male rabbits and 21.5% for females.

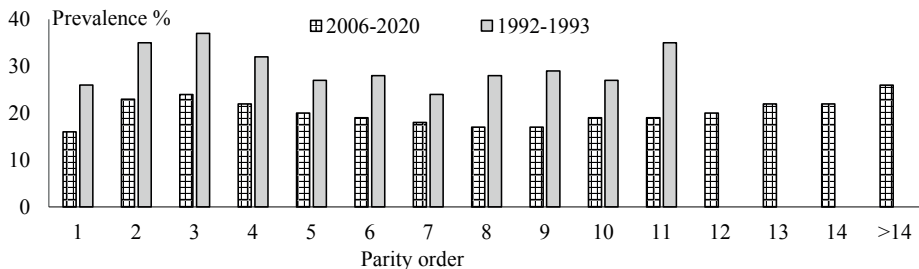


Figure 8: Prevalence of rhinitis and parity order in 50 230 females individually examined in 265 farms from 2006 to 2020, and 4719 females checked in 94 farms during 1992-1993 (Badiola *et al.*, 2000).

**Table 5:** Effect of the gender and genetic type of farmed breeding rabbits on the prevalence of clinical rhinitis (PrCR) from 1996 to 2020, in Spain and Portugal.

Gender	Rabbit line	Farms n	Cohorts n	Sampled rabbits n	PrCR %	X <sup>2</sup>	P-value	OR
Male	H	54	177	3 624	20.8	115	P<000.1	0.34
Male	S	16	51	1 032	43.4	184	P<000.1	2.13
Female	H	283	1 258	67 799	12.2	4 129	P<000.1	0.43
Female	S	93	329	18 641	48.7	10 187	P<000.1	4.50

H: Healthiest rabbit line, S: Sickest rabbit line, X<sup>2</sup>: Chi-squared test, OR: Odds Ratio.

The correlation coefficient between the prevalence of CR in males and females was 0.55. In a previous observational study during 1992 and 1993, prevalence was also higher in males: 42.9% compared to 30.8% in females (Badiola *et al.*, 2000).

### Effect of gender and rabbit line on the prevalence of rhinitis

Table 5 shows the joint evaluation of gender and line over the prevalence of rhinitis.

Table 5 shows the results for the males and females related with the highest (more susceptible rabbit line to rhinitis and *sickest*) and lowest (*healthiest line*) prevalences of rhinitis. They were quantified by risk ratios, with pronounced influence of the rabbit line. The results between genders of the sickest rabbit line, described above, are apparently contradictory, because in this case, the males were less sick than the females. This bias may be because of differences between the numbers and mainly the origin (AI centres vs. farms) of cohorts checked in these analyses. Genital diseases have also been described as manifestations of pasteurellosis (Renault, 1981; Harcourt-Brown, 2017).

### Prevalence of clinical atrophic rhinitis in farmed rabbits

After the reports by DiGiacomo *et al.* (1989) and Frymus *et al.*, (1991), we were interested in checking the occurrence of atrophic rhinitis in Iberian farms. The 5th database included 37 396 lactating does. We found 5872 with CR; of these, 15 had atrophic rhinitis (15/37 396: 0.04%). Of 22 247 males, we diagnosed rhinitis in 5016 rabbits and the atrophic form in 25 cases (0.11%). In total there were 40 breeding rabbits manifestly affected, out of a total of almost 60 000 adults individually examined. This was not a relevant pathologic issue in farmed rabbits. Prevalence was not determined previously, according to Barthold *et al.* (2016). In relation to the *pathologic study of atrophic rhinitis in rabbits*, we evaluated young and adult rabbits affected by atrophic rhinitis from outbreaks in 3 farms. At the external inspection, we observed dirty wet nostrils and a deviated snout; this issue was better observed at the subcutaneous inspection of the head (Figure 3). Internal examination showed nasal septum deviation, with an off-white mucopurulent exudate in the nasal mucous, sometimes affecting nasal or ethmoid turbinates mucosa, or in both, unilateral or bilateral. Besides, we observed atrophy of nasal turbinates or ethmoid turbinates. Histologically, infiltrated heterophils could be observed on and in epithelium and lamina propria. Many lymphocytes and plasma cells were also observed in the lamina propria.

### Results of the microbiological studies

In Table 6 we show the results obtained from sampled lesions, not necessarily compatible with respiratory processes, for example mastitis or dermatitis. We wanted to mix the results of lesions and the aetiology, mainly with *Pasteurella* spp. and *Staphylococcus* spp.

In this database there were 158 *P. multocida* isolates and 16 *P. canis*; Stahel *et al.* (2009) found 5% of *P. canis*. Besides, there were 229 samples with *S. aureus*, 10 with *S. xylosum*, 3 with *S. sciuri*, 3 coagulase-negative staphylococci, and 11 isolates with other *Staphylococcus* spp. We have not studied unapparent carriers of *Pasteurella* spp. or *Staphylococcus aureus* as in the studies by DiGiacomo *et al.* (1991) and Attili *et al.* (2020), respectively. Table 6 shows the main causality of *Pasteurella* spp. in otitis, followed by pneumonia and the decrease in favour of staphylococci. Concerning otitis, we mainly examined cases of otitis externa. Flatt *et al.* (1977), analysed cases of the suppurate form, in young and adult rabbits, with the main aetiology due to *Pasteurella* spp. Di Castri *et al.* (2021) evaluated 215 cases

**Table 6:** Pathogens isolated in 444 samplings from 153 rabbit farms during 2001 – 2020.

Sampled lesion	N	<i>Pasteurella</i> spp. N	%	<i>Staphylococcus</i> spp. N	%	Other
Otitis media, externa	11	9	81.8	2	18.2	-
Pneumonia, pleuritis	103	65	63.1	30	29.1	*
Rhinitis <sup>1</sup> , sinusitis	105	56	53.3	46	43.8	**
Metritis, pyometra	29	12	41.4	14	48.3	***
Subcutaneous abscess	24	7	29.2	17	70.8	-
Purulent conjunctivitis	13	3	23.1	10	76.9	-
Mastitis, acute, chronic	101	21	20.8	80	79.2	-
Ulcerative pododermatitis	23	1	4.3	22	95.7	-
Pustular dermatitis	35	0	0	35	100	-
Total	444	174		256		12

<sup>1</sup>. Including 5 samples of atrophic rhinitis. \* Four *Bordetella bronchiseptica* isolates, 1 *Streptococcus* spp., 1 *Klebsiella pneumoniae*, 1 *Escherichia coli* and 1 *Salmonella* spp. \*\* Two *B. bronchiseptica* isolates (simultaneous with *S. aureus*) and 1 *Streptococcus pneumoniae*. \*\*\* Two *Salmonella* spp. isolates and 1 *Trueperella pyogenes*.

of otitis media in the laboratory, of which 94.4% also had rhinitis or pneumonia, among others. *P. multocida* was the only agent isolated in 83/110 samples, in addition to 13/110 also with *S. aureus*. Internal otitis is underdiagnosed on farms, unless it is suppurate, or the affected rabbit also has head tilt (Mancinelli and Lennox, 2017). Kunstýř and Naumann (1985) stated that otitis in farmed rabbits is mainly due to *P. multocida*, unlike in pet rabbits, in which *Encephalitozoon cuniculi* predominates. In relation to other pathogens isolated in samples of respiratory processes sent to the lab, *Bordetella bronchiseptica* isolates were infrequent. This differs from studies related to farmed (Deeb *et al.*, 1990) or pet (Jekl, 2021) rabbits. Other pathogens are more likely to be identified in research studies, as was the case of Villa *et al.* (2001), though a notable effort has been made to know more about *P. multocida*, the most common agent in rabbit infectious airway disorders (García-Álvarez *et al.*, 2015; Massacci, *et al.*, 2018; Zhu *et al.*, 2020, among others).

## CONCLUSIONS

From this 25-yr retrospective study on commercial rabbit farms, the mean annual prevalence of CR (95%) in lactating does was 19.9% (19.7-20.1%). Prevalence improved from 29.6% in 1996 to 15% in 2020. This outcome may be taken as a usefulness baseline threshold for on-farm assessments, though ranges vary considerably. Our study highlights a key factor of rhinitis: the rabbit line. In addition, median parity order was 5; more resilient rabbit lines are required, amongst other changes, to increase their lifespan. Besides, males were more prone to having rhinitis than females; this different susceptibility should be studied. With regard to the enabling risk factors of rhinitis, season had a marked effect. In our latitude, morbidity was higher in summer than winter. Environmental factors are paramount in sustainable rabbit production. Its effect on rabbit health should be better known, and applied in practice. In this study we have observed a clear effect of service timing on the female's health. The suitable strategy for control of respiratory diseases should be focused first on prevention, addressing the underlying effect of risk factors. As a beneficial result, antimicrobials will be used less and will be more efficient.

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