Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

HUMORAL AND CELL-MEDIATED IMMUNE RESPONSES OF BEEF AND DAIRY CATTLE EXPERIMENTALLY INFESTED WITH *PSOROPTES OVIS*

Jean-François Lonneux[1], Thu Queen Nguyen[1], Wim Hollanders[4], Martine Denis[2], Etienne Thiry[3], Pierre Paul Pastoret[2], Bertrand Losson[1]

Supported by the Institut pour l'Encouragement de la Recherche Scientifique dans l'industrie et l'Agriculture (1RSIA grants 5463A and 5580A) and the Merck Sharp and Dohme Company.
The authors thank J. Detry, A. Henry, and H. Gianfreda for technical assistance.

[1]Departments of Parasitology and Pathology of Parasitic Diseases, Faculty of Veterinary Medicine, University of Liège, Liège
[2]Immunology and Vaccinology, Faculty of Veterinary Medicine, University of Liège, Liège
[3]Virology and Pathology of Viral Diseases, Faculty of Veterinary Medicine, University of Liège, Liège
[4]Belgium; and Schering Plough Animal Health, Rue de Stalle, 67, B-1180, Brussels, Belgium

ABSTRACT

Objective : To compare cellular and humoral immune responses of beef (Belgian White and Blue [BWB]) and dairy (Friesian-Holstein [FH]) cattle to *Psoroptes ovis* infestation and to determine whether *P ovis* infestation impaired immune responses to infectious bovine rhinotracheitis virus (IBR) vaccine or an immunogenic protein (keyhole-limpet hemocyanin [KLH]).

Animals : 19 BWB and 6 FH 1-year-old calves.

Procedure : 2 trials were performed. In each trial, 7 (trial 1) or 6 (trial.2) BWB calves and 3 FH calves were experimentally infested with *P ovis* and 3 BWB calves were maintained as uninfested controls. Animals were inoculated with KLH and IBR virus vaccine twice; 3 BWB calves in each trial were treated with ivermectin. Serum antibody responses to KLH, IBR virus, and *P ovis* were measured by use of ELISA. A lymphocyte transformation assay was used to determine nonspecific responses to 3 mitogens and specific lymphocyte reactivity to *P ovis* antigen.

Results—In each trial, 3 BWB and 3 FH calves developed clinical signs of psoroptic mange and mites could be recovered. Infested and control animals developed similar antibody titers to KLH and IBR virus. Antibodies to *P ovis* were detected early in some infested calves, and this was correlated with a marked cell-mediated immune response. Lymphocyte responsiveness to the 3 mitogens was not significantly different among groups.

Conclusions : In these calves, infestation with *P ovis* induced a marked humoral and cell-mediated immune response. Immunosuppression was not evident. (*Am J Vet Res* 1998;59:583-587)

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

Psoroptes ovis infestations have a marked economic impact on the beef cattle industry[1-2]; however, in Belgium, the disease is rarely observed in dairy7 cattle,[3] and dairy cattle were not involved in any of the more than 1,000 outbreaks of psoroptic mange in the United States between 1974 and 1979.[4] Fisher and Wright[5] studied differences in susceptibility to *P ovis* between Brahman and Hereford calves and concluded that resistance of Brahman cattle was attributable to behavioral, rather than immunologic, factors, but few data are available on differences among cattle breeds in regard to susceptibility to *P ovis* infestation. The purpose of the study reported here was to compare cellular and humoral immune responses of beef (Belgian White and Blue [BWB]) and dairy (Friesian Holstein [FH]) cattle to *P ovis* infestation and to determine whether P ovis infestation modified the ability to mount a specific immune response against unrelated antigens.

Materials and Methods

ANIMALS

Nineteen BWB and 6 FH calves were used. The BWB calves had been born in the experimental unit of the Faculty of Veterinary Medicine, whereas FH calves were purchased from a single dairy farm. All calves received colostrum from a herd free of **infectious bovine rhinotracheitis (IBR)** virus infection and were housed in individual boxes in a parasite-free environment for at least 4 months prior to the start of the trial.

All calves were 1 year old at the start of the trial. They were fed hay ad libitum and commercial pelleted feed. Rations were calculated to obtain growth of approximately 0.85 kg/d. Calves were tied but able to groom themselves. All calves were treated with an organophosphate[a] 3 weeks prior to the study.

EXPERIMENTAL PROCEDURE

For technical reasons, it was not possible to perform a single trial. Consequently, 2 similar trials were performed with a 1-year interval between trials. For each trial, 3 BWB calves were randomly selected and allocated to an uninfested control group. Three FH calves and 7 (trial 1) or 6 (trial 2) BWB calves were assigned to an infested group. For trial 1, calves in the infested group were infested on day 0 with 600 adult *P ovis* mites collected as described,[6] from a donor animal isolated at the study site and with an additional 100 mites on day 28. For trial 2, calves in the infested group were infested on day 0 with 600 adult P ovis mites. On day 56 (trial 1) or 35 (trial 2), all calves were vaccinated against IBR virus infection[b] and were inoculated with purified keyhole-limpet hemocyanin (KLH,[c] 2 mg, SC) in incomplete Freund adjuvant. On day 77 (trial 1) or 63 (trial 2), 6 BWB calves in each trial were blocked according to severity of skin lesions, and 3 calves were randomly selected and treated with ivermectin[d] (200 µg/kg of body weight, SC). Calves were booster

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

vaccinated against IBR virus infection and inoculated with KLH a second time on day 98 (trial 1) or 77 (trial 2).

CLINICAL EVALUATION

For trial 1, mite counts were determined and clinical index scores reflecting severity of infestation were assigned on days 56 and 98 (ie, when calves were vaccinated against IBR virus infection). For trial 2, mite counts were performed and clinical indices were assigned on days 35, 63, and 98 (ie, when calves were initially vaccinated against IBR virus infection, when calves were treated with ivermectin, and 3 weeks after calves were booster vaccinated against IBR virus infection). Mite counts were determined by examining skin scrapings harvested from 3 areas at the periphery of the lesions at a magnification of 30 times.[6] Living *P ovis* mites were collected and counted. Additionally, affected areas were delineated on a standardized map. This allowed calculation of the percentage of affected skin (clinical index).[6] Body weight was measured weekly, and weekly weight gains were determined. Total and differential WBC counts were determined weekly.

EVALUATION OF HUMORAL IMMUNE RESPONSES

Serum antibody responses to KLH and IBR virus were determined weekly, and antibody responses to *P ovis* were determined every other week, except that for trial 2, antibody responses to *P ovis* were determined weekly from day 0 to day 35. Serum antibody responses to IBR virus were determined by use of a commercially available ELISA[e]; results were expressed, according to the manufacturer's recommendations, as the ratio of absorbance units for the analyzed serum sample to absorbance units for a standard serum sample. Antibody responses to KLH were also determined by use of an ELISA. Briefly, microtitration plates[f] were coated overnight with 100 µl/well of a solution containing 10 µg of KLH/ml diluted in carbonate buffer (15 mM Na_2CO_3, 35 mM $NaHCO_3$, pH 9.6). Plates were blocked with horse serum diluted 1:100 in the same buffer and washed 3 times with phosphate-buffered saline (0.9% NaCl) solution containing 0.5% tween 20 (PBSS-TWEEN). Test sera (100 µl) diluted 1:100 in PBSS-TWEEN containing the blocking agent were deposited in triplicate, and plates were incubated at 37 C for 1 hour. Plates were again washed 3 times, and 100 µl of rabbit anti-bovine IgG conjugated to horseradish peroxidases and diluted 1:1,000 was added to each well. Plates were again incubated for 1 hour at 37 C and washed 3 times, and 100 pl of substrate (1,2 phenylene-diamine,[g] 2 mM H_2O_2, 0.1M citric acid, 0.2M Na_2HPO_4, pH 5.0) was added to each well. The reaction was stopped after 10 minutes with a solution of sulfuric acid (6M), and optical densities (OD) were measured with a microplate reader.[h] Results were expressed as percentages, using the following formula: 100 X (OD_S - OD_{nc}) / (OD_{PC} - OD_{NC}) where OD_S is the OD of the sample and OD_{NC} and OD_{PC} are the OD of negative and positive control serum standards, respectively. Negative and positive control serum standards were serum samples collected prior to the first inoculation and 7 days after the second inoculation of a 2-year-old FH heifer given KLH twice, 21 days apart.

Serum antibody responses to *P ovis* were determined by use of an anti-P *cuniculi* sandwich ELISA.[6] Results were expressed as the reciprocal of the test serum dilution that yielded an OD equal to

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

OD_{NC} + 0.25 X (OD_{PC} — OD_{NC}), where OD_{NC} and OD_{PC} were the OD of negative and positive control samples tested on the same plate, respectively. Titers less than 400 were assigned a score of 0, whereas titers between 400 and 1,600, 1,600 and 6,400, 6,400 and 25,600, and 25,600 and 102,400 were assigned scores from 1 to 4, respectively. Titers greater than 102,400 were assigned a score of 5.

EVALUATION OF CELLULAR IMMUNE RESPONSES

Lymphocyte proliferative responses to phytohemagglutinin (PHA), concanavalin A (ConA), and pokeweed mitogen (PWM) and specific lymphocyte reactivity to P ovis antigen were assessed every 2 weeks, as described.[7] Blood samples were collected between 9 and 10 am and anticoagulated with heparin (10 U of heparin/ml of blood). Twenty-microliter aliquots of PBSS (negative control), ConA (1 µg/well), PWM (0.125 and 1 µg/well in trials 1 and 2, respectively), PHA (0.125 µg/ well), and *P cuniculi* antigen, obtained as described[7] (5 and 1.5 µg/well in trials 1 and 2, respectively) were added in triplicate to cultures of blood mononuclear cells (2 X 10^6 cells/200 pl). Optimal concentrations of mitogens and antigen were determined from preliminary assays. Cell cultures were incubated for 90 hours at 37 C in a humidified atmosphere containing 5% CO_2. Cultures were then pulsed with tritiated thymidine (0.25 µCi/well) and incubated for an additional 18 hours. Cells were collected on glass fiber pads, using a cell harvester, and the amount of radioactive thymidine incorporated was measured.

Results were compared with those for unstimulated control cultures. Response to *P cuniculi* was expressed as a stimulation index (SI), calculated by dividing mean count/min for the stimulated culture by mean count/min for the control culture. Mean SI for infested calves was calculated as a percentage of the mean SI for control calves (ie, mean SI for the control calves was considered to be 100%). Responses to PHA, ConA, and PWM were expressed as the change in counts per minute (ΔCPM), calculated by subtracting mean count/min for control cultures from mean count/min for stimulated cultures. A single batch of each mitogen and antigen was used throughout, each trial.

STATISTICAL ANALYSIS

Calves were grouped according to breed (BWB vs FH) and status (control, exposed and infected [ie, developed gross skin lesions with live mites], exposed but not infected [ie, no skin lesions and no mites]). Body weight, weight gain, serum antibody responses, lymphocyte proliferative responses, and specific lymphocyte reactivity to *P ovis* were compared among groups by use of ANOVA. Lymphocyte reactivity to *P ovis* was considered significantly different from that for control calves when SI was outside the 95% confidence interval for mean SI for control calves.

To study the effect of ivermectin treatment, data for infested BWB calves were also analyzed by use of two-way ANOVA. For all analyses, a value of $P \leq 0.05$ was considered significant.

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

Results

MITE COUNTS AND CLINICAL INDICES

Skin lesions were first observed 3 (trial 1) and 2 (trial 2) weeks after infestation with adult *P ovis*. Three of 7 (trial 1) and 3 of 6 (trial 2) BWB calves developed extensive dermatitis with scabs, and mites could be recovered from these 6 calves throughout the study. The other 7 BWB calves that were infested with niites did not develop skin lesions or developed only localized lesions from which no or only, a few living mites were obtained (Tables 1 and 2).

In trial 1, FH calves were mildly affected (clinical index < 1% of total body surface and mite counts that were low or 0), whereas in trial 2, FH calves were severely affected. In trial 1, mite counts and clinical indices for control calves were 0. One control calf in trial 2 was accidentally infested; mite count was 26 and clinical index was 3.1% on day 98. Mite counts and clinical indices for the other 2 control calves were 0.

HUMORAL IMMUNE RESPONSE TO IBR VIRUS AND KLH ANTIGENS

After immunization, serum antibody response to IBR was immediately increased in all animals. Two weeks after the first immunization, all animals were seropositive; results were unchanged after booster vaccination. Significant differences were not detected among groups at any time during the study, and ivermectin treatment did not affect antibody response to IBR. Serum antibody response to KLH increased after the first inoculation. After 2 weeks, response decreased but increased again after the second inoculation. Significant differences were not detected among groups at any time during the study.

Table 1. *Specific antibody responses to Psoroptes ovis in calves infested with adult mites on day 0 (trial 1)*

	Antibody titer									Mite count		Clinical index (%)	
Calf n°	D0	D14	D28	D42	D56	D70	D84	D98	D112	D56	D98	D56	D98
Belgian White and Blue calves													
1*	0	0	1	1	3	3	4	3	3	10	0#	3,7	2,6
2*	0	0	0	0	2	5	5	5	ND	6	1	4,3	7,7
3*	0	0	1	3	4	5	4	5	5	> 500	16	8,8	20
4t	0	0	0	0	0	0	0	0	0	0	0#	0	0
5t	0	0	0	0	0	2	0	0	0	0	0	0	0

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

6t	0	0	1	1	1	1	1	1	1	1	0#	0	0,2
7t	0	1	1	1	1	1	1	1	1	1	0	0	0
Friesian-Holstein calves													
8	0	0	0	0	0	1	1	1	1	0	0	0	0
9	0	0	0	0	0	0	0	0	0	2	0	0,1	0,05
10	0	0	0	1	2	3	2	1	1	10	0	0,3	0,3

Légende de la figure. ***** Infested with mites and developed skin lesions; **t** infested with mites but did not develop skin lesions; teal ves treated with invermectin on day 77. **ND** = not determined.

Table 2.*Specific antibody responses to P ovis in calves infested with adult mites on day 0 (trial 2)*

	Antibody titer											Mite count			Clinical index (%)		
Calf n°	D0	D7	D14	D21	D28	D35	D49	D63	D77	D91	D98	D35	D63	D98	D35	D63	D98
Belgian White and Blue calves																	
1*	0	1	3	3	3	4	4	5	4	4	4	650	196	0#	3,4	15	0
2*	0	0	2	2	3	3	4	4	5	4	4	470	30	0	6,9	17	6,9
3*	0	1	2	3	3	4	4	1	3	3	3	41	6	0#	1,7	2,3	0
4t	0	0	0	0	0	0	1	1	0	0	0	3	0	0#	0,1	0	0
5t	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6t	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Friesian-Holstein calves																	
7	0	0	1	3	3	4	5	5	5	5	5	520	383	16	7	22	10
8	0	0	0	0	0	0	1	2	3	4	4	0	83	6	0	0,3	3,1
9	0	0	0	1	1	2	3	3	3	3	3	340	83	115	3,1	2	3,4

Légende de la figure. *****Infested with mites and developed skin lesions; **t**infested with mites but did not develop skin lesions; **#**calves treated with invermectin on day 63.

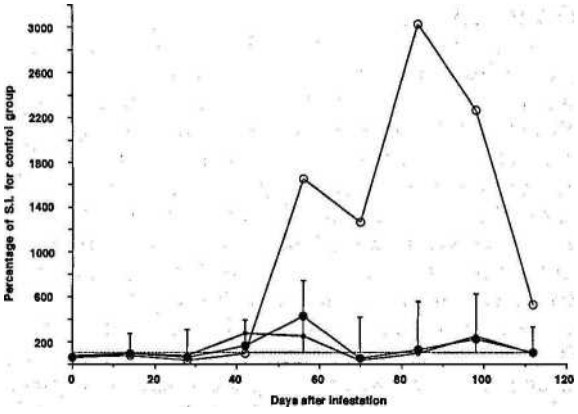
Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

Table 3. *Mean ± SEM daily weight gain in calves experimentally infested with P ovis mites and in control calves*

	Belgian white and blue calves			
Trial n°	Control	Affected	Unaffected	Frieslan - Holstein calves
1*	952 +/- 11 (n=3)	796 +/- 149 (n=3)	876 +/- 64 (n+4)	1,074 +/- 56 (n=3)
2t	820 +/- 130 (n=3	720 +/- 160 (n=3)	1,230 +/- 90 (n=3)	740 +/- 90 (n=3)

Légende de la figure. *Data collected from day 0 through 77; tData collected from day 0 through day 63.

Figure 1. *Titre de la figure Specific lymphocyte reactivity to Psoroptes ovis antigen (measured as stimulation index) in Belgian White and Blue (BWB) calves infested with P ovis that developed skin lesions (O), BWB calves infested with P ovis that did not develop skin lesions (•), and Friesian- Holstein calves (•) infested with P ovis in trial 1. Mean stimulation index for 3 control calves is given bars represent the 95% confidence interval for the control group.*



WEIGHT GAIN

In both trials, exposed and experimentally infested calves had a significantly lower mean daily weight gain than did control calves. However, mean body weight and mean cumulated weight gain were not significantly different among groups at any time during the study (Table 3).

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

HUMORAL IMMUNE RESPONSES

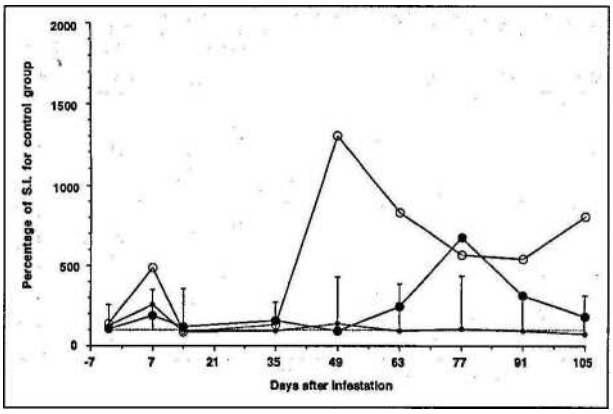
All but 1 of the control animals were seronegative (ie, titer score = 0) for antibodies against *P ovis* at the beginning of the study. The remaining control animal (trial 2) was considered seropositive throughout the study (titer score = 1). In trial 1, 1 control animal became seropositive (titer score = 1) on day 84. In trial 2, the control calf that was accidentally infested became seropositive on day 77 (titer score = 2). Infested BWB calves that developed skin lesions first became seropositive on day 28 (trial 1) or day 7 (trial 2). In both groups, antibody titers gradually increased until day 70 or 63 and remained high thereafter. Infested BWB calves that did not develop skin lesions were seronegative most of the time; nevertheless, 4 of 7 were seropositive (titer score $\geq$ 1) at least once during the study. In the first trial, 2 of 3 FH calves became seropositive. In trial 2, all 3 FH calves became seropositive (Tables 1 and 2). Mean WBC counts remained within reference limits throughout the study. In the first trial, 1 heavily infested calf had a transient increase in WBC count (25,350 cells/µl) with eosinophilia.

CELLULAR IMMUNE RESPONSES

In trial 1, mean SI of infested BWB calves that developed skin lesions was significantly different from mean SI of control calves from day 56 onward. Mean SI of infested BWB calves that did not develop skin lesions and of FH calves were not significantly different from mean SI of control calves. In trial 2, mean SI of infested BWB calves that developed skin lesions was significantly greater than mean SI of control calves on day 7 after infestation and from day 49 onward. Mean SI of FH calves was significantly higher than mean SI of control calves on day 77.

Mean ΔCPM of infested BWB calves that devel-, oped skin lesions was greater than mean ΔCPM of control calves throughout the study for all 3 mitogens. Ivermectin treatment did not affect ΔCPM.

Figure 2. *Specific lymphocyte reactivity to Povis antigen (measured as stimulation index) in trial 2. See Figure 1 for key.*



Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

Discussion

Hyperkeratosis is one of the main pathologic features in histologic sections from *P ovis*-infested calves[8] and from human beings with severe Sarcoptes scabiei infestation.[9] In people with *S scabiei* infestation, hyperkeratosis generally is associated with an underlying immunodeficiency (eg, acquired immunodeficiency syndrome, leukemia, use of immunosuppressive drugs, or Down's syndrome),[10] and similarities between hyperkeratotic lesions in human beings and lesions associated with *P ovis* in cattle suggest that an immunological defect could explain differences in susceptibility to *P ovis* infestation among cattle. In vitro blastogénic responses of lymphocytes to mitogens are reduced in rabbits infested with *P cuniculi*,[11,12] and T- cell responsiveness to PHA and ConA mitogens is decreased in cattle infested with P ovis.[13] However, it is not clear whether these alterations are a result of the mites themselves or are secondary to restraint of animals. Moreover, suppression of host immune function could not explain the hyperglobulinemia.[14] the development of a strong specific humoral response,[15] or the myeloid hyperplasia[16] that have been found. Additionally, for severely infested calves, in vitro lymphocyte response to mitogens was found to increase,[17] whereas for adult cows, a significant variation in lymphocyte responsiveness to mitogens was not found[7] in the present study, *P ovis* infestation did not impair mitogen-induced lymphocyte proliferation, and humoral and cellular immune responses to a commercial vaccine and an immunogenic protein were similar in infested and control animals. Nevertheless, weight gain of infested calves was less than that of control calves, confirming previous reports[2,18,19] that *P ovis* infestation has an effect on the metabolism of calves.

If hyperkeratosis in *P ovis*-infested animals is not a result of immunosuppression, it could be related to the large numbers of mites in such lesions and to mechanical disruption of the horny layer caused by mites' activity.[20,21] Hyperkeratosis could be explained as a complex dermoepidermal reaction that results in activation of the immune system.[22]

The immune system can be activated very rapidly after *P ovis* infestation. In the present study, development of a specific lymphoblastic response to *P ovis* antigen was detectable as soon as 7 days after infestation. This was probably related to the intensity of exposure to mite antigens. Expressing exposure in cumulative mite days, Davis and Moon[23] demonstrated a correlation between exposure and delayed hypersensitivity response in S scabiei-infested animals. The delay in development of a specific lymphoblastic response in trial 1 versus trial 2 could have been related to a poorer initial exposure (eg, because of scratching by trial animals) or to a difference in the activity of the mite strains used in each trial.

High specific antibody titers were apparently unable to control parasite populations in these calves. Development of hyperkeratosis in *P ovis*-infested animals could be related to development of a strong but poorly effective or inadequate response that allowed development of large populations of mites, which in turn, induced hyperkeratosis.

Fundamental differences in development of humoral and cellular immune responses were not detected between FH and BWB calves. This suggests that differences in susceptibility of the 2 breeds is not secondary to immunosuppression in BWB cattle. However, subtle differences in secretion of

Published in : American Journal of Veterinary Research (1998), vol. 59, n°5, pp. 583-587
Status : Postprint (Author's version)

lymphokines have been found in animals with parasitic diseases, and this could, at least in part, explain the results of the present study. Further work is required to check this hypothesis.

Légende :

[a] Phoxim-Sarnacuran, Bayer, Leverkusen, Germany.

[b] Duphavac IBR/PI3, Fort Dodge Animal Health, Weesp, The Netherlands.

[C] Sigma Chemical So, St Louis, Mo.

[d] Ivomec injectable, Merial, Rahway, NJ.

[e] IBR ELISA, Bio-X, Brussels, Belgium.

[f] Linbro, ICN, Costa Mesa, Calif.

[8] Dako A/S, Glostrup, Denmark.

[h] Microplate autoreader EL 309, Bio-Tek Instruments Inc, Winooski, Vt.

References

1. Pouplard L, Losson B, Detry M. et al. Les gales bovines. Ann Med Vet 1990;134:531-539
2. Lonneux J-F, Nguyen TQ, Detry J, et al. A study of the relationship between daily weight gains, mites counts, antibody titer and lesions in *Psoroptes ovis* infested cattle. Vet Parasitai 1998;in press.
3. Lonneux J-F, Losson B. Epidémiologie des gales bovines. Ann Med Vet 1996;140:317-327.
4. Hourrigan JL. Spread and detection of psoroptic scabies of cattle in the United States. J Am Vet Med Assoc 1979;175:1278-1280.
5. Fisher WF, Wright FC. Susceptibility of scabies-naive Hereford and Brahman calves to *Psoroptes ovis* infestations. Southwest Entomol 1981;6:57-61.
6. Lonneux J-F, Nguyen TQ, Hollanders W, et al. A sandwich enzyme-linked immunosorbent assay to study the antibody response against *Psoroptes ovis* in cattle. Vet Parasitai 1996;64:299-314.
7. Losson B, Detry-Pouplard M, Pouplard L. Haematological and immunological response of unrestrained cattle to *Psoroptes ovis*, the sheep scab mite. Res Vet Sci 1988;44:197-201.
8. Stromberg PC, Guillot FS. Pathogenesis of psoroptic scabies in Hereford heifer calves. Am J Vet Res 1989;50:594-601.
9. Van Neste DJ. Human scabies in perspective. Int J Dermatol 1988;27:10-15.
10. Davis DP, Moon RD. Dynamics of swine mange: a critical review of the literature. J Med Entomol 1990;27:727-737.
11. Wikel SK. Immunomodulation of host responses to ectoparasite infestation—an overview. Vet Parasitai 1984;14:321-339.
12. Uhlir J. Humoral and cellular immune response of rabbits to Psoroptes cimiculi, the rabbit scab mite. Vet Parasitai 1991;40:325- 334.
13. Pruett JH, Guillot FS,- Fisher WF. Humoral and cellular immunoresponsiveness of stanchioned cattle infested with *Psoroptes ovis*. Vet Parasitai 1986;22:121-133.
14. Fisher WF, Crooshank HR. Effects of *Psoroptes ovis* (Acarina: Psoroptidae) on certain biochemical constituents of cattle serum. Vet Parasitai 1982;11:241-251.
15. Fisher WF. Development of serum antibody activity as determined by enzyme-linked immunosorbent assay to *Psoroptes ovis* (Acarina: Psoroptidae) antigens in cattle infested with *P ovis.* Vet Parasitai 1983;13:363-373.
16. Stromberg PC. Bone marrow response in cattle with chronic dermatitis caused by *Psoroptes ovis.* Vet Pathol 1987;24:365-370.
17. Stromberg PC, Fisher WF, Guillot FS, et al. Systemic pathologic responses in experimental *Psoroptes ovis* infestation of Hereford calves. Am J Vet Res 1986;47:1326-1331.
18. Fisher WF, Wright FC. Effects of the sheep scab mite on cumulative weight gains in cattle. J Econ Entamai 1981;74:234-237.

19. Cole NA, Guillot FS. Influence of *Psoroptes ovis* on the energy metabolism of heifer calves. Vet Parasitai 1987;23:285-295.

20. Arlian LG, Runyan RA, Achar S, et al. Survival and infestivity of *Sarcoptes scabiei* var. *canis* and var. *hominis*. J Am Acad Dermatol 1984;11:210-215.

21. Van Neste DJ , Staquet MJ. Similar epidermal changes in hyperkeratotic scabies of humans and pigs. Am J Dermatopathol 1986;113:267-273.

22. Van Neste DJ. Scabies in the pig as a model of human scabies with special reference to the hyperkeratotic form of the disease process. Models Dermatol 1987;3:170-179.

23. Davis DP, Moon RD. Density of itch mite, *Sarcoptes scabiei* (Acari: Sarcoptidae) and temporal development of cutaneous hypersensitivity in swine mange. Vet Parasitai 1990;36:285-293