Lesions Induced in the Nasal Turbinates of Neonatal Pigs Inoculated with Pasteurella multocida and/or Bordetella bronchiseptica

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ABSTRACT. Specific-pathogen-free (SPF) neonatal pigs were intranasally inoculated with serotype D strains of Pasteurella multocida and/or strain L3 of Bordetella bronchiseptica, and their lesions were studied. Marked inflammatory changes were observed only after the infection with B. bronchiseptica. Both organisms were constantly recovered from the nasal cavities of the pigs during the experimental period; B. bronchiseptica was recovered in higher numbers than P. multocida. Degeneration and resorption of trabeculae in varying grades were observed in all the inoculated pigs. The turbinate bone lesions induced by P. multocida were characterized by the following changes: slight resorption of trabeculae by osteocytic osteolysis, active osteoid synthesis near trabeculae and periosteum due to increase of osteoblasts, and enhanced new bone formation. In many areas of the trabeculae, the trabeculae had been replaced by the proliferative osteoblasts and osteoids, thus, none of the pigs showed gross signs of swine atrophic rhinitis (AR). In contrast, the lesions induced by B. bronchiseptica were severe resorption of trabeculae by osteoclastic osteolysis, perforating resorption, increase of fibrous tissue near trabeculae, and impaired osteogenesis due to the damage to the osteoblasts. Thus, all the pigs showed severe gross signs of AR. Hence, quality and severity of the lesions observed between the 2 species of the bacteria were apparently different. Co-infection of the pigs with the 2 species of the bacteria apparently enhanced the turbinate lesion formation. Our observations are consistent with the hypothesis that B. bronchiseptica alone is responsible for pathogenesis of swine AR. The different mechanisms in pathogenesis by the 2 species of the bacteria in relation to the production of characteristic turbinate lesions are discussed.—KEY WORDS: atrophic rhinitis, Bordetella bronchiseptica, Pasteurella multocida, swine nasal turbinate.

Swine atrophic rhinitis (AR) is a disease characterized by severe necrosis of epithelia of the upper respiratory tract and by deformity and reduction both in volume and size of the nasal turbinate and snouts [5, 15, 25]. Fetter et al. [7, 8] reported that the primary lesion induced in the trabeculae of the neonatal pigs affected with the disease was osteoporosis due to decreased bone formation by the degenerative osteoblasts and osteocytes, and they considered that resorption of the bone adjacent to the degenerative bone cells may have contributed to the overall loss of bone. Similar observations were reported by others [12, 18], though some differences in the formed bone lesions both in quality and severity were noted among different studies. There has been a substantial amount of evidence supporting that Bordetella bronchiseptica is a major cause of the disease [2, 5, 7, 8, 12, 14, 15, 25, 31, 33], although many bacteria and/or factors responsible for the occurrence of swine AR have been suggested. Some studies positively suggested that demonecroic toxin (DNT) of B. bronchiseptica may act as an active component to produce the turbinate atrophy in neonatal pigs [11] or in young mice [29].

Certain strains belonging to a capsular serotype [3] D or A of Pasteurella multocida
Table 1. Experimental design

<table>
<thead>
<tr>
<th>Group</th>
<th>P. multocida</th>
<th>B. bronchiseptica</th>
<th>No. tested</th>
<th>Age in days at inoculation</th>
<th>PID(^e) necropsy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP-72</td>
<td>5x10^7(^a)</td>
<td>-</td>
<td>4</td>
<td>7</td>
<td>49</td>
</tr>
<tr>
<td>A</td>
<td>5x10^7</td>
<td>-</td>
<td>4</td>
<td>7</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>15x10^7</td>
<td>-</td>
<td>4(^b)</td>
<td>7, 14, 21</td>
<td>63(^c)</td>
</tr>
<tr>
<td>B</td>
<td>-</td>
<td>5x10^4</td>
<td>4</td>
<td>7</td>
<td>49</td>
</tr>
<tr>
<td>C</td>
<td>5x10^7</td>
<td>5x10^4</td>
<td>4</td>
<td>7</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td>15x10^7</td>
<td>5x10^4</td>
<td>4</td>
<td>7</td>
<td>63</td>
</tr>
<tr>
<td>D (Control)</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>(70)(^d)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Total viable cell numbers (i.e., CFU).
\(^b\) Inoculated 3 times at 1-week-intervals.
\(^c\) Days after the primary inoculation.
\(^d\) Days of age at necropsy.
\(^e\) Postinoculation days.

are also capable of producing DNT [4, 9, 30]. Difference was not observed between the P. multocida DNT and B. bronchiseptica DNT in their biologic and toxic properties [17]. A close correlation was demonstrated by de Jong et al. [4] between the pathogenicity of P. multocida in swine AR and the ability of the organisms to produce DNT. Additional studies have implicated the toxigenic strains of P. multocida as a causative agent for swine AR [13, 22, 23, 26, 27]. In some studies, however, in which the turbinate lesions were induced in neonatal pigs, inoculations of toxigenic strains of P. multocida were preceded application of acetic acid or inoculation of B. bronchiseptica [22, 23, 26, 27].

The purpose of the present investigation was to compare the lesions induced in the nasal turbinates of pigs by the toxigenic serotype D strains of P. multocida with those induced by B. bronchiseptica.

MATERIALS AND METHODS

Bacteria and culture media: Pasteurella multocida capsular serotype D strains SP-72 [17] and 47459 (provided by Dr. de Jong, Central Veterinary Institute, Rotterdam, The Netherlands) and Bordetella bronchiseptica strain L3 [11] of pig origins were used. These strains produced DNT and were preserved as lyophilized cultures. Yeast extract-proteose peptone-cystine (YPC) agar medium [21] and Bordet-Gengou’s (BG) agar medium [1] supplemented with 20% horse blood were used for propagation of P. multocida and B. bronchiseptica, respectively, throughout the study.

Neonatal pigs: Specific-pathogen-free (SPF) neonatal pigs, seven days of age, derived from 4 sows were used. These pigs were removed immediately at the birth from their dams and housed in a separate room in each infection group (Table 1). They were fed only sterile milk (Nippon Formula Feed Manufacturing Corp., Tokyo, Japan) without any antibiotics during the experimental period. Prior to the experiment, serum and nasal swab samples of each pig were collected, and these samples were checked serologically and bacteriologically for the presence of P. multocida and B. bronchiseptica infections according to the methods and the criteria described previously [24, 30, 32].

Preparation of inocula: Pasteurella multocida organisms grown on the YPC agar
plates for 6 hr at 37°C were harvested and suspended in 0.02 M phosphate-buffered solution, pH 7.0, containing 0.85% NaCl (PBS). Viable cells of the suspension were adjusted to approximately $5 \times 10^7$ colony-forming units (CFU)/0.5 ml by spectrophotometry ($10^{10}$ cells/ml = optical density at 650 nm of 0.386) with a model 6/20 spectrophotometer (Coleman Instruments). Phase I of *B. bronchiseptica* [20] grown on the BG agar plates for 18 hr at 37°C was collected and suspended in PBS. Viable cells of the suspension were adjusted to approximately $5 \times 10^4$ CFU/0.5 ml by spectrophotometry. Inoculation was done within 30 min after the inocula was prepared.

**Experimental infection:** Experimental design is summarized in Table 1. Inoculation of *P. multocida* and/or *B. bronchiseptica* in neonatal pigs was performed via the nasal route by using syringe. These pigs were divided into 4 groups randomly distributed in regard to the origin: A, inoculation of *P. multocida* (12 pigs from 4 sows); B, inoculation of *B. bronchiseptica* (4 pigs from 4 sows); C, co-inoculation of the 2 species of the bacteria (8 pigs from 4 sows); and D, control (2 pigs from 2 sows). Among the 12 pigs in group A, 4 pigs were inoculated 3 times with the same dose of the 47459 inoculum at 1 week intervals. All the pigs were bled and sacrificed postinoculation days (PID) 49 or 63.

**Clinical observation:** Clinical signs of individual neonatal pigs, such as sneezing and coughing, were recorded daily during the experimental period. Gross lesions of AR characterized by shortening and deviation of the snouts in these pigs were graded at necropsy on a basis of 0 to 3 (0=normal, 1=mild, 2=moderate, and 3=severe). The pigs with the scores of 2 and 3 were considered as positive clinical AR.

**Bacterial isolation:** Isolation of *B. bronchiseptica* and *P. multocida* was attempted at PID 7, 21, 49, or 63 from the nasal cavity of each neonatal pig as follows: Two cotton swab samples were obtained from each pig. One sample (about 0.1 g/sample) was directly streaked both on the YPC and BG agar plates. The other sample was suspended in 1 ml of PBS. Two fold serial dilutions were made in each 1 ml volume of PBS, and then 0.1 ml portions of each dilution were streaked both on YPC and BG agar plate. The viable cell numbers (CFU) were counted after the incubation for 10 (YPC) or 18 (BG) hr at 37°C. Numbers of the organisms (CFU/g of sample) were averaged in each infection group, and the result was expressed on a basis of $-\rightarrow++$ (−=no recovery, +=<10^2 CFU, ++=<10^6 CFU, and +++=>10^6 CFU). Identification of the recovered organisms was done by the criteria described previously [24, 32]. The DNT-producing ability of the recovered *P. multocida* or *B. bronchiseptica* was investigated in guinea pigs, according to the procedure described in a previous report [17].

**Serologic examination:** Serum samples collected from individual neonatal pigs at necropsy were investigated by the rapid plate agglutination (RPA) [19] test with strain L3 of *B. bronchiseptica* and the indirect hemagglutination (IHA) [3] test with strain SP-72 of *P. multocida*.

**Macroscopic observation of the nasal cross section:** The nasal cross sections cut at a middle level between the canine and the first premolar teeth were obtained from the pigs within one hr after euthanasia. The nasal turbinate atrophy and distortion of the nasal septum were macroscopically evaluated and scored on a basis of 0 to 4 by using these cross sections, according to the criteria described by Maeda et al. [12]. The scores above 2 were considered as "positive" atrophy.

**Histologic examination:** The examination was carried out on the transverse sections of the snout mentioned above. Tissues were fixed in 10% neutral formalin solution, decalcified in 15% ethylenediaminetetraacetic acid
solution, pH 7.3, at 37°C for 96 hr, dehydrated in alcohol, and embedded in paraffin. They were cut into thin sections approximately 6 μm thick, which were stained with hematoxylin and eosin (H & E), Masson’s trichrome, or phosphotungstic acid hematoxylin (PTAH).

RESULTS

Clinical findings: None of the pigs in group A that were given P. multocida alone (group B) or those that were given both P. multocida and B. bronchiseptica (group C), respectively. These pigs showed moderate to severe lesions of AR at necropsy. All the controls in group D remained clinically normal during the period.

Recovery of the organisms: The inoculated organisms were recovered from the nasal cavities of all the infected pigs (Table 3). From all the pigs in group A, the toxigenic P. multocida was constantly recovered in small numbers during the experimental period. B. bronchiseptica, phase I, was recovered constantly in abundant numbers from all the pigs in group B throughout the period. Both B. bronchiseptica and P. multocida were recovered constantly in abundant numbers from all the pigs in group C during the period. Bacterial isolations from control animals (group D)

Table 2. Gross lesions of neonatal pigs inoculated intranasally with P. multocida or B. bronchiseptica or both

<table>
<thead>
<tr>
<th>Group</th>
<th>No. tested</th>
<th>Clinical AR</th>
<th>Nasal turbinate atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Score range</td>
<td>No. positive</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>0 (0.0) b)</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>2–3 (2.25)</td>
<td>4</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>3 (3.0) c)</td>
<td>8</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
</tbody>
</table>

a) See Table 1.
b) Shortening and deviation of the snout was grossly evaluated (0=normal, 1=mild, 2=moderate, and 3=severe). Scores 2 and 3 were considered as positive clinical AR. Mean in ratherness.
c) Macroscopically evaluated and scored, according to the criteria described by Maeda et al. [12]. Scores above 2 were considered as positive.

Table 3. Recovery of the inoculated organisms from the nasal cavities of the neonatal pigs that were given P. multocida or B. bronchiseptica or both intranasally

<table>
<thead>
<tr>
<th>Group</th>
<th>No. tested</th>
<th>P. multocida</th>
<th>B. bronchiseptica</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre</td>
<td>PID 7</td>
</tr>
<tr>
<td>A</td>
<td>12</td>
<td>0 b)</td>
<td>12 (+)</td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>0</td>
<td>0 (−)</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>0</td>
<td>2 (−)</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>0</td>
<td>2 (−)</td>
</tr>
</tbody>
</table>

a) See Table 1.
b) No. cases with positive recovery.
c) Grade of bacterial recovery. See in the text.
were negative for the 2 species of the bacteria during the period.

**Determination of antibodies:** All the pigs used were serologically negative for both *B. bronchiseptica* and *P. multocida* prior to the inoculation. Antibodies against *P. multocida* were not detected by the IHA test in all the pigs at necropsy. Antibodies against *B. bronchiseptica* in varying degrees were detected by the RPA test in all the pigs in group B and C. Controls were seronegative for the both species of the bacteria.

**Macroscopic findings:** No gross lesion was found in the nasal cross sections of all the pigs in group A (Table 2). In contrast, moderate to severe nasal turbinate atrophies were induced in all the pigs in groups B and C. The lesions induced in the group C were generally more severe than those induced in the pigs in group B. The nasal turbinates of the controls were normal.

**Histologic lesions induced by *P. multocida***: Nasal mucosa: The infected nasal mucosa in group A showed essentially normal structure, and most of the epithelial cells appeared intact with cilia. Turbinate bones: Slight reduction of the trabeculae both in volume and size was observed in all cases, and the lesions seemed to be induced by degeneration and resorption of trabeculae due to osteocytic osteolysis (Fig. 1). No increase in number of osteoclasts was noted as compared with that of controls. Osteoclastic osteolysis was rarely observed, however, most of the osteoclasts appeared to be degenerative. Marked proliferation of osteoblasts and osteoid synthesis in varying stages near trabeculae and periosteum resulted in further new bone formation (Fig. 2), and the trabeculae were replaced by proliferating osteoblasts and osteoids. In many areas, such osteoid tissues were surrounded by a mass of osteoblasts. Increase of fibrous tissue near the periosteum was apparent. The turbinate le
sions induced in all the 12 pigs in group A were closely resembled.

Histologic lesions induced by B. bronchiseptica: Nasal mucosa: Marked degeneration and degenerative detachment of the epithelial cells were noted in all the pigs in group B, and cilia were lost from most of the epithelial cells. Marked hyperplasia of the epithelial cells was also observed in many parts of the epithelium, and a moderate number of lymphocytes and neutrophils infiltrated in the epithelium. Turbinate bones: The volume and size of the trabeculae were markedly reduced compared with those of controls, and these lesions seemed to be induced by degeneration and resorption of trabeculae mainly due to perforating resorption or osteoclastic osteolysis (Fig. 3). Osteoclastic cells were markedly increased in numbers in all the cases. Most of the cells in trabeculae were necrotic, and trabeculae were replaced by the proliferating fibrous tissues (Fig. 4). Slight increase of osteoblasts was found near trabeculae, however, most of them were undergoing severe necrotic changes (Fig. 5). Slight osteoid synthesis was also observed near trabeculae. Bone formation in their trabeculae was scarcely observed due to the damage to their osteogenesis, probably by impairing the osteoblasts. The turbinate lesions induced in all the 4 pigs in group B were closely resembled.

Histologic lesions induced by co-infection with the 2 species of the bacteria: The changes induced in all the 8 pigs in group C (Fig. 6) were closely resembled to those induced by B. bronchiseptica (Figs. 3–5). However, the changes induced by the mixed infections were somewhat more severe than
Fig. 5. Ventral turbinate core of a pig in group B given *B. bronchiseptica* alone, at PID 49. Many pyknotic osteoblasts are observed around the rarefied trabeculae (small arrows). Some osteoclasts are phagocytizing the degenerative osteoblasts (large arrow). H & E stain; $\times 350$.

Fig. 6. Ventral turbinate core of a pig in group C that was given both *B. bronchiseptica* and *P. multocida* intranasally, at PID 63. Many osteoclasts are noted in contact with the rarefied bony trabeculae (small arrows). Marked proliferation of osteoblasts and fibroblasts is observed beneath the periosteum. Some osteoblasts are pyknotic (large arrows). H & E stain; $\times 350$.

Fig. 7. Ventral turbinate core of a control pig in group D euthanatized at 70 days of age. Showing normal structure. H & E stain; $\times 87.5$.

those induced by *B. bronchiseptica* alone.

*Histologic findings in controls:* The nasal mucosa of all the pigs in group D appeared normal (Fig. 7). Trabeculae were significantly larger in volume and size than those of the pigs in groups A, B, and C. In some parts of trabeculae, slight osteocytic osteolysis and resorption of trabeculae by osteoclasts were noted. Active osteoid synthesis by the osteoblasts, a normal osteogenesis in the growing neonatal pigs, was observed in many parts of trabeculae.
DISCUSSION

Pasteurella multocida was first associated with swine AR by Gwatkin and Dzenis [10], but its pathogenic role has never been definitely established; experimental infections of the pigs with the organism have frequently failed to reproduce the disease. Since de Jong et al. [4] suggested the presence of the DNT-producing strains among the P. multocida isolated from AR cases, the toxigenic strains and its DNT have been considered by some European researchers as a major causative agent and a virulent factor, respectively, in swine AR [6, 13, 22, 23, 26, 27]. P. multocida does not colonize itself on the nasal mucosa under natural and experimental conditions [9, 27], therefore, these workers employed a chemical irritation [6, 23] or B. bronchiseptica infection [13, 22, 26, 27] prior to the exposure to the toxigenic strains of P. multocida. The first aim of the present investigation was characterization of the histologic lesions induced in the nasal turbinates of the pigs that were given P. multocida or B. bronchiseptica alone to clarify the aetiological roles of the 2 species of the bacteria in the development of swine AR. The quality and severity of lesions observed between the 2 species of the bacteria were apparently different, and the present observations are consistent with the hypothesis that B. bronchiseptica is responsible for pathogenesis of swine AR.

Recently, Pedersen and Elling reported that the toxigenic serotype D [23] or serotype A [6] P. multocida strains induced swine AR which was characterized by the initial bone resorption by osteoclastic osteolysis accompanied by impaired osteogenesis in an early stage of the infection (within PID 14). The turbinate lesions in their experiments were similar to those of naturally occurring AR, hence, they concluded that the strains are able to induce the nasal turbinate atrophy in neonatal pigs. In contrast to their observation, the present investigation showed that the intranasal inoculation of P. multocida alone (infection group A) resulted in the characteristic turbinate lesions at PID 49 or 63 including the following changes; slight resorption of trabeculae by osteocytic osteolysis, active osteoid synthesis beneath the osseous cores and periosteum due to increase of osteoblasts, and enhanced new bone formation. Many areas of the trabeculae have been replaced by thus proliferating osteoblasts and osteoids. Hence, macroscopically the nasal turbinates of the pigs were essentially normal, and none of these pigs showed clinical AR. The difference in quality of the formed turbinate lesions observed in the 2 studies can not be explained by the different experimental conditions and factors involved in the 2 tests, such as observation period, pre-treatment with acetic acid, strains employed, preparation of inocula, and proliferation of the organisms on the nasal mucosa. Further confirmation of the present results by an independent study is needed.

Pasteurella multocida DNT has been emphasized as a factor responsible for the pathogenesis of swine AR [4, 6, 13, 22, 23, 26, 27]. Elling and Pedersen [6] and Pedersen and Elling [23] stated that the P. multocida DNT may interfere with the physiological regulation of the development of the osseous core of the nasal turbinates in neonatal pigs. The nasal cross sections removed from neonatal pigs were cultured in a medium containing P. multocida or its purified DNT [18], and the lesions induced in these organ cultures were found very similar to those induced in vivo by P. multocida alone (unpublished data). Thus, it seems that P. multocida DNT is capable of producing the characteristic turbinate histologic lesions as mentioned above. Evidence is apparent that P. multocida DNT enhances osteoid synthesis both in vivo and in vitro. The mechanism of P. multocida DNT responsible for the osteoid synthesis is interesting to investigate. We concluded, therefore, that the toxigenic P.
multocida strains were responsible for the turbinate lesion formation characteristic to the bacterium, but probably not able to induce swine AR.

Pedersen and Barford [22] and Rutter et al. [28] reported that the intranasal inoculation of neonatal pigs with B. bronchiseptica induced a transient atrophy of the nasal turbinates, but that the severe lesions observed in naturally occurring AR were not reproduced experimentally with B. bronchiseptica alone. In contrast, Elling and Pedersen [6] and Pedersen and Elling [23] demonstrated in SPF neonatal pigs that the toxigenic P. multocida strains are capable of inducing a disease comparable with naturally occurring swine AR and that the pathogenesis of the nasal turbinate atrophy involves both impaired osteoblastic bone formation and enhanced osteoclastic bone resorption. Interestingly, the turbinate bone lesions observed by them [6, 23] were very similar to those induced by B. bronchiseptica alone (infection group B) in our study. Inflammatory reaction was not observed in the P. multocida infected nasal mucosa [6, 23], whereas severe chronic catarhral inflammatory changes were observed in the B. bronchiseptica infected ones. The turbinate lesions induced by B. bronchiseptica were very similar to those described previously in the nasal turbinates of the pigs that were given B. bronchiseptica [2, 8, 11, 12, 14, 15, 25, 31, 33]. In addition, the lesions induced in the nasal cross sections cultured in a medium containing B. bronchiseptica or its purified DNT were also similar to those induced in vivo by B. bronchiseptica alone (unpublished data). B. bronchiseptica DNT apparently impaired osteoblastic bone formation by damaging the osteoblasts resulting in enhancement of osteoclastic bone resorption. The present findings support the previous hypothesis [11] that B. bronchiseptica DNT is a major virulent factor of the organisms for pathogenesis of swine AR.

Infection with B. bronchiseptica followed by infection with the toxigenic P. multocida caused a progressive AR corresponding to the disease observed in the field [22, 27]. The observations were confirmed by the present study in infection group C. The phenomenon may be interpreted as follows: Both species of the bacteria colonize on the nasal mucosa, producing an abundant amount of DNT by autolysis of the cells [16]. The osteoclastic and osteolytic bone resorption enhanced by co-infection with the 2 species of the bacteria may be overcome by the osteoid synthesis promoted by P. multocida DNT. In addition, impaired osteoblastic bone formation observed in groups B and C may enhance the production of severe nasal turbinate atrophy in the pigs.

P. multocida DNT and B. bronchiseptica DNT located intracellularly in viable organisms [16]. The DNT was not secreted from the actively growing cells. A low amount of cell-free DNT was detected in the culture supernatants after autolysis of the cells. Experimental studies have shown that B. bronchiseptica well colonizes on the nasal mucosa and causes severe chronic catarhral inflammatory reaction [33], whereas P. multocida establishes poorly on the normal nasal mucosa without causing much damage to the mucosa [9, 15, 27]. These findings were consistent with those of the present studies, suggesting the different ability of the 2 species of the bacteria in production of DNT in vivo. Our preliminary study showed that the nasal mucosa cultured in vitro in the presence of the purified DNT of P. multocida or B. bronchiseptica were equally injured by the toxin. These observations also supported our present hypothesis that P. multocida is probably not able to induce clinical swine AR. In conclusion, B. bronchiseptica is a known causative agent for swine AR and its DNT is responsible for pathogenesis of the nasal turbinate atrophy.
REFERENCES


要約

*Pasteurella multocida* および *Bordetella bronchiseptica* の単独あるいは混合接種により形成された SPF 新生豚の鼻甲介病変: 小山田敏文・吉川 優・清水まき子・中井豊次1)・久米脇己2)（北里大学獣医畜産学部獣医病理学教室。1)北里研究所柏葉医学研究所。2) 北里研究所）— *Pasterella multocida* (Pm) SP−72 株および 47459 株と *Bordetella bronchiseptica* (Bb) L3 株を 1 過節 SPF 豚の鼻甲介に単独あるいは混合接種し、7 あるいは 9 過後病変を計測観察を行った。両菌は実験初期中鼻腔より回収されたが、回収菌数は Bb がはるかに多く、炎症性変化も Bb 接種豚で明らかであった。Pm 接種豚の鼻甲介は肉眼変状を示さず、組織学的には骨細胞性骨融解による骨梁の吸収が存在するものの、活発に増生した骨芽細胞と類骨に置換していた。これに対し、肉眼的に明らかに萎縮が認められた。Bb 接種豚の鼻甲介には破骨細胞性骨融解による重度の穿孔性骨梁吸収が認められ、同時に骨芽細胞障害による骨新生の減弱と骨梁周辺の線維増生を伴っていた。Pm. Bb を混合接種した場合の骨梁変化は Bb 接種のそれよりも重度であった。以上の成績から両菌の鼻甲介に対する病原性は明らかに異なり、AR 病変の形成は主に Bb で展開されることが強く示唆された。