Synergistic effects of concurrent challenge with bovine respiratory syncytial virus and 3-methylindole in calves

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Objective—To evaluate the potential synergy between bovine respiratory syncytial virus (BRSV) and 3-methylindole (3MI) in inducing respiratory disease in cattle.

Animals—20 mixed-breed beef calves.

Procedure—A 2 × 2 factorial design was used, with random assignment to the following 4 treatment groups: unchallenged control, BRSV challenge exposure (5×10^4 $TCID_{50}$ by aerosolization and 5.5×10^5 $TCID_{50}$ by intratracheal inoculation), 3MI challenge exposure (0.1 g/kg of body weight, PO), and combined BRSV-3MI challenge exposure. Clinical examinations were performed daily. Serum 3MI concentrations, WBC counts, PCV, total plasma protein, and fibrinogen concentrations were determined throughout the experiment. Surviving cattle were euthanatized 7 days after challenge exposure. Pulmonary lesions were evaluated at postmortem examination.

Results—Clinical respiratory disease was more acute and severe in cattle in the BRSV-3MI challenge-exposure group than in cattle in the other groups. All 5 cattle in this group and 3 of 5 cattle treated with 3MI alone died or were euthanatized prior to termination of the experiment. Mean lung displacement volume was greatest in the BRSV-3MI challenge-exposure group. Gross and histologic examination revealed that pulmonary lesions were also most severe for cattle in this group.

Conclusions and Clinical Relevance—Feedlot cattle are commonly infected with BRSV, and 3MI is produced by microflora in the rumen of all cattle. Our results suggest that there is a synergy between BRSV and 3MI. Thus, controlling combined exposure may be important in preventing respiratory disease in feedlot cattle. (*Am J Vet Res* 1999;60:563–570)

Bovine respiratory disease (BRD) is an economically important disease syndrome of beef cattle.[1,2] Many infectious agents have been associated with this multifactorial disease complex.[3] However, little attention has been paid to potentially important noninfectious causes or to possible interactions between infectious and noninfectious causes of BRD.

Three-methylindole (3MI) is a documented cause of respiratory disease in cattle. **Acute bovine pulmonary emphysema and edema (ABPE)** can be induced by 3MI toxicosis and is typically observed in mature cattle that have been moved from poor quality pastures to lush, green pastures that are rich in tryptophan.[4,5] Lactobacilli in the rumen convert dietary tryptophan to 3MI, which is rapidly absorbed into the systemic circulation. Three-methylindole acts specifically in pulmonary tissues through cytochrome-dependent mixed function oxidase and prostaglandin H synthetase found in the smooth endoplasmic reticulum of type-I pneumonocytes and Clara cells.[6] Conjugation produces free radicals and causes oxidative damage to pulmonary tissues, causing interstitial emphysema, edema, type-II pneumonocyte hyperplasia, and hyaline membrane formation.[6] Dyspnea, tachypnea, respiratory distress, and acute death can be observed in affected animals within 14 days after dietary changes.[7] Similar syndromes have been documented in association with exposure to other toxic compounds, such as 4-ipomeanol and Perilla mint ketone.[8,9]

Young cattle entering feedlots also undergo dietary changes that may influence 3MI production. These cattle typically are moved from pasture in late summer and offered feedlot rations with high concentrations of tryptophan. Production of 3MI may increase in rumen lactobacilli, causing subclinical pulmonary damage in these calves similar to that seen in cattle with ABPE. Oxidative damage to airways may allow opportunistic viral and bacterial pathogens to invade and cause clinical BRD.

Clinical and postmortem findings in cattle with ABPE are similar to those in feedlot cattle with pneumonia attributed to **bovine respiratory syncytial virus (BRSV)** infection.[7,10,11] Feedlot cattle with pneumonia

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