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Impact of Mycoplasma hyopneumoniae and Lawsonia intracellularis on the performance of pigs divergently selected for feed efficiency

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Abstract
Feed efficiency (FE) is a valuable trait, yet how genetic selection for enhanced FE affects other processes such as response to disease is unknown. Disease from endemic respiratory and enteric pathogens such as Mycoplasma hyopneumoniae (Mh) and Lawsonia intracellularis (LI) are common in swine production. Therefore, the aim of this study was to examine if pigs selected for high versus low FE based on residual feed intake (RFI) respond differently to a dual respiratory and enteric challenge. Pigs selected for low RFI (LRFI, high feed efficiency) pigs are considered more FE compared to their high RFI (HRFI, low feed efficiency) selected counterparts. Using a 2 x 2 factorial design, 25 littermate pairs from the HRFI and 25 littermate pairs from the LRFI line (barrows, 50 ± 7 kg BW) were selected, with one pig from each pair assigned to individual pens in either the challenge or the non-challenge (control) rooms (n = 25 barrows per line/challenge). On days post inoculation (dpi) 0, the challenged pigs were inoculated with LI and Mh (MhLI). Feed intake, body weight, fecal swabs, and serum samples were collected and recorded weekly for 42 days. On dpi -2 and 47, 14 littermate pairs (n=7 barrows per line/challenge) were utilized for initial and final body composition scans using dual X-ray absorptiometry to calculate longitudinal whole body tissue accretion rates for lean, protein, fat, and bone mineral content. Serum antibody levels and fecal shedding of LI were used to confirm infection. Control pigs remained negative by all measures during the 6 week trial and MhLI inoculated pigs were confirmed positive via serological antibody responses by dpi 14 for LI and Mh. There were no interactions between RFI line and challenge status for any overall performance parameter ($P > 0.05$). The six week MhLI challenge resulted in a 17% reduction in ADG, a 12% reduction in ADFI, and a 7% reduction in G:F versus controls ($P < 0.05$). In addition, compared to the control pigs, MhLI challenge reduced lean, protein, and lipid accretion rates by 16% ($P < 0.05$). Genetic selection for high FE resulted in decreased ADFI and increased G:F ($P < 0.01$), but did not impact ADG or tissue accretion versus low FE pigs. Collectively, these results demonstrate that a dual enteric and respiratory pathogen challenge reduced ADG, ADFI, G:F and tissue accretion in growing pigs. Further, there was no evidence that selection for enhanced FE based on RFI index affects response to disease.

Keywords
Lawsonia intracellularis, Mycoplasma hyopneumoniae, pig, feed efficiency

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Running Head: Growth performance of MhLI infected pigs

Impact of *Mycoplasma hyopneumoniae* and *Lawsonia intracellularis* on the performance of pigs divergently selected for feed efficiency[1]

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ABSTRACT: Feed efficiency (**FE**) is a valuable trait, yet how genetic selection for enhanced FE affects other processes such as response to disease is unknown. Disease from endemic respiratory and enteric pathogens such as *Mycoplasma hyopneumoniae* (**Mh**) and *Lawsonia intracellularis* (**LI**) are common in swine production. Therefore, the aim of this study was to examine if pigs selected for high versus low FE based on residual feed intake (**RFI**) respond differently to a dual respiratory and enteric challenge. Pigs selected for low RFI (**LRFI**, high feed efficiency) pigs are considered more FE compared to their high RFI (**HRFI**, low feed efficiency) selected counterparts. Using a 2 x 2 factorial design, 25 littermate pairs from the HRFI and 25 littermate pairs from the LRFI line (barrows, 50 ± 7 kg BW) were selected, with one pig from each pair assigned to individual pens in either the challenge or the non-challenge (control) rooms (*n* = 25 barrows per line/challenge). On days post inoculation (**dpi**) 0, the challenged pigs were inoculated with LI and Mh (**MhLI**). Feed intake, body weight, fecal swabs, and serum samples were collected and recorded weekly for 42 days. On dpi -2 and 47, 14 littermate pairs (*n*=7 barrows per line/challenge) were utilized for initial and final body composition scans using dual X-ray absorptiometry to calculate longitudinal whole body tissue accretion rates for lean, protein, fat, and bone mineral content. Serum antibody levels and fecal shedding of LI were used to confirm infection. Control pigs remained negative by all measures during the 6 week trial and MhLI inoculated pigs were confirmed positive via serological antibody responses by dpi 14 for LI and Mh. There were no interactions between RFI line and challenge status for any overall performance parameter ($P > 0.05$). The six week MhLI challenge resulted in a 17% reduction in ADG, a 12% reduction in ADFI, and a 7% reduction in G:F versus controls ($P < 0.05$). In addition, compared to the control pigs, MhLI challenge reduced lean, protein, and lipid accretion rates by 16% ($P < 0.05$). Genetic selection for high FE resulted in decreased ADFI and increased G:F ($P < 0.01$), but did not impact ADG or tissue accretion versus low FE pigs. Collectively, these results demonstrate that a dual enteric and respiratory pathogen challenge reduced ADG, ADFI, G:F and tissue accretion in growing pigs. Further, there was no evidence that selection for enhanced FE based on RFI index affects response to disease.

Keywords: Lawsonia intracellularis, Mycoplasma hyopneumoniae, pig, feed efficiency

INTRODUCTION

Diminished pig performance due to compromised respiratory and enteric health is an economic, animal welfare, and antimicrobial use concern facing pork producers worldwide. Two pathogens with considerable economic impact in grow-finish pigs are *Mycoplasma hyopneumoniae* (**Mh**) and *Lawsonia intracellularis* (**LI**). *Mycoplasma hyopneumoniae* is the primary causative agent of enzootic pneumonia, a bacterial disease prevalent in all production stages (Sibila et al., 2009; Thacker and Minion, 2012). *Lawsonia intracellularis* is an enteric bacterium that causes porcine proliferative enteropathy, a disease resulting in thickened intestinal mucosa (McOrist and Gebhart, 2012). With both pathogens, ADFI and ADG are attenuated, increasing production costs (Brandt et al., 2010; Thacker and Minion, 2012).

With immune challenge from disease agents, nutrients are partitioned towards the immune response components resulting in antagonized performance (Johnson, 2012). Variation in the ability of pigs to allocate nutrients for immune system function and recovery may dictate how pigs resolve a pathogen challenge. It was hypothesized that selection for increased feed efficiency (**FE**), an economically important trait, makes pigs more susceptible to immunological stressors due to a reduced ability to repartition nutrients for recovery (Rauw, 2007). However, inflammatory challenges have not supported this hypothesis thus far (Rakhshandeh et al., 2012; Labussière et al., 2015; Merlot et al., 2016). In examining response to disease, high FE pigs were more robust during a Porcine Reproductive and Respiratory Syndrome (**PRRS**) virus challenge than pigs of lower FE (Dunkelberger et al., 2015), although these differences were small.

Thus, the aim of this study was to determine if high FE pigs would be at a disadvantage, in terms of growth performance, compared with pigs of lower FE during a dual enteric and respiratory challenge, using divergent residual feed intake (**RFI**) lines to model selection for FE.

MATERIALS AND METHODS

All animals were handled in accordance with the Iowa State University Institutional Animal Care and Use Committee (IACUC# 6-16-8298-S).

Animals, Housing, and Experimental Design

A total of 25 low RFI (**LRFI**) and 25 high RFI (**HRFI**) littermate pairs of unvaccinated Yorkshire barrows (50 ± 7 kg BW) from the 11th generation of the Iowa State University RFI selection project were chosen for this experiment. The two lines have been divergently selected such that pigs with low RFI (LRFI) consume 12-15% less feed for a given amount of growth and backfat as pigs with greater RFI (Boddicker et al., 2011). Thus LRFI pigs are considered more FE compared to their HRFI selected counterparts (Cai et al., 2008). These pig lines can be utilized to evaluate the physiology that may define FE differences in growing pigs. Therefore, littermate pairs were split, randomly allocated to individual pens across two rooms in the same barn, and allowed to acclimate for 21 days prior to inoculation. During the 21-day acclimation period, pooled serum and fecal samples were tested to confirm the

selected pigs were negative for both Mh and LI based on antibody response and fecal PCR, respectively. All pigs had free access to water and were fed *ad libitum* the same corn-soybean diet for the duration of the experiment. The diet (Table 1) was formulated to meet or exceed all nutritional requirements for pigs of that size (National Research Council, 2012).

Prior to inoculation, one room was designated the control room and the other the challenge room. The resulting 2 x 2 factorial design consisted of four experimental groups: 1) LRFI control (*n* = 25 barrows), 2) HRFI control (*n* = 25 barrows), 3) LRFI-MhLI challenged (*n* = 25 barrows), and 4) HRFI-MhLI challenged (*n* = 25 barrows). The rooms had identical pen size, feeders, flooring, heating, cooling, and water supply, but separate manure pits. Temperature was recorded daily in both rooms, and there was no difference in temperature measurements between the two rooms. Additionally, there were no performance differences between the rooms during the 21-day acclimation period prior to the challenge (data not shown).

Inoculation and Sample Collection

On days post inoculation (**dpi**) 0, pigs (67.83 ± 1.929 kg BW) in the challenge room were inoculated with both Mh and LI (**MhLI;** challenge pigs), while pigs in the control room were inoculated with a sham (Control pigs). Pigs were under snare restraint for all inoculations. For the respiratory challenge, Mh was dosed in a 10 mL Mh inoculum (strain 232, containing 10^5 color-changing units/mL) via intra-tracheal gavage and for the enteric challenge, pigs were intra-gastrically gavaged with 40 mL LI inoculum (2 mL gut homogenate, containing 2 x 10^7 LI organisms). Both inoculums were prepared at the Iowa State University Veterinary Diagnostic Laboratory (**ISUVDL,** Ames, IA). The Mh inoculum was prepared from a crude lung homogenate and the LI from crude gut homogenates.

Individual feed disappearance and BW were recorded for each pig on dpi 0 and then weekly for the duration of the 6 week challenge period (dpi 42). From these recordings, ADG, ADFI and G:F were calculated for each week. At dpi 21, 12 littermate pairs (*n* = 6 barrows/line/challenge) were removed and euthanized for separate experimentation that will be described elsewhere; their removal was accounted for in the statistical model. Additionally, these pigs were utilized to evaluate lungs and ileum which re-confirmed successful inoculation, which will be reported elsewhere (data not shown).

Blood samples (10 mL) were collected into BD Vacutainer serum tubes (Becton, Dickinson and Company, Franklin Lakes, NJ) via jugular venipuncture from all pigs at dpi 0, 14, 21, 28 and 42. Samples were allowed to clot, centrifuged (2,000 x *g* for 10 minutes at 4^{o}C), and serum collected and stored at -80^{o}C. Individual pig serum samples were submitted to the ISUVDL and tested via ELISA tests to quantify Mh (IDEXX Laboratories, Inc., Westbrook, ME) and LI (SVANOIR® Ileitis ELISA, Boehringer Ingelheim Svanova, Uppsala, Sweden) antibody response. *Lawsonia intracellularis* antibody response was reported as percent inhibition, in which inhibition between 20 and 30% was considered suspect for LI, and inhibition greater than 30% was considered positive. *Mycoplasma hyopneumoniae* antibody response was reported as a sample to positive (**S:P**) ratio. A S:P ratio between 0.30 and 0.40 was considered suspect for Mh and an S:P greater than 0.40 was considered positive for Mh.

Fecal swabs were collected on a randomly selected subset of 14 littermate pairs (7 barrows per line/challenge) at dpi 0, 7, 14, 21, 28, 35 and 42 to asses fecal shedding of LI. Swabs were submitted to the ISUVDL for routine quantitative real-time PCR (**RT-PCR**) testing for presence of LI shedding (Burrough et al., 2015). Polymerase chain reaction cycle-threshold (**Ct**) values less than 35 were considered positive for LI presence and greater than 35 were interpreted as negative. Pigs with fecal samples that have lower Ct values are more likely to have clinical signs, gross lesions or microscopic lesions or lesions, such that Ct values less than 20 would be consistent with clinical disease, samples with Ct values between 20 and 25 are likely infected with microscopic lesions, and those with Ct values between 26 and 35 are usually asymptomatic without discernible lesions, but still must respond immunologically.

Whole body composition and tissue accretion rates

The same subset of 14 littermate pairs (*n* = 7 pigs/line/challenge) that were randomly chosen prior to inoculation for fecal swab testing were also utilized for longitudinal assessment of whole body composition and tissue accretion rates over the six week MhLI challenge period. Pre- (initial, dpi -2) and post-challenge (final, dpi 47) whole body composition was measured using non-destructive dual-energy X-ray absorptiometry (**DXA**; Hologic Discovery A, Bedford, MA), as previously described (Suster et al., 2003). To minimize gut fill, feed was unavailable for 12 hours prior to the scan. Pigs were transported off-site for the scans and returned the same day to their individual pens. For the initial DXA scan, pigs were anesthetized via an intramuscular injection of telazol:xylazine:ketamine cocktail (4.4, 4.4, and 2.2 mg/kg BW respectively). Once anesthetized, pigs were placed prone on the DXA scan table, with the fore and hind legs extended. After the scan was complete, pigs were given time to recover from anesthesia and were then moved back to their pens. For the final body composition, pigs were euthanized via captive bolt. Whole body, bone, and lean tissue mass, and fat mass and percentage were provided by the raw DXA scans. Data from the raw DXA output was then adjusted to account for blood volume and gut fill using calibration curves that were built as previously described (Colpoys et al., 2016; Curry et al., 2017). These longitudinal scan data were then used to calculate tissue accretion rates (g/d) from corrected DXA scan results using the following formula:

$$\text{g/d} = \frac{\text{(corrected final scan measurement – corrected initial scan measurement)}}{\text{days between scans}}$$

Statistical analysis

The SAS program was used for the statistical analyses of all performance and tissue accretion data (SAS Institute Inc., Cary, NC). The following mixed model with a repeated statement was fitted to ADG, ADFI, G:F, antibody response, and LI fecal shedding data:

$$Y_{ijklmno} = \mu + MhLI_i + Line_j + Period_k + Litter\{Line\}_{il} + Age_m + BWstart_n + (MhLI \times Line)_{ij} + (MhLI \times Period)_{ik} + (Line \times Period)_{jk} + (MhLI \times Line \times Period)_{ijk} + e_{ijklmno}, \quad (1)$$

wherin $Y_{ijklmno}$ = the phenotype measured on animal n;

$MhLIe_i$ = effect of disease challenge i (fixed effect; MhLI, Control);

$Line_j$ = effect of genetic line j (fixed effect; low RFI, high RFI);

$Period_k$ = effect of period k (fixed effect; dpi 0-7, 8-14, 15-21, 22-28, 29-35, 35-42); $Litter\{Line\}_{il}$ = effect of litter l nested within line i (random effect);

Age_m = covariate effect of age m (regression coefficient);

$BWstart_n$ = covariate effect of BW at the start of the trial;

$(MhLI \times Line)_{ij}$ = interaction effect between challenge i and line j;

$(MhLI \times Period)_{ik}$ = interaction effect between challenge i and period k;

$(Line \times Period)_{jk}$ = interaction effect between line j and period k;

$(MhLI \times Line \times Period)_{ijk}$ = interaction effect between challenge i and line j and period k; and

$e_{ijklmno}$ = error term of animal n subjected to challenge i, of line j, in period k, born in litter l, of age m, $e_{ijklmno} \sim NID(0, \delta^2_e)$.

Period was identified as the repeated effect in the model for each individual. The following variance-covariance structures for repeated measures were evaluated to describe the individual data on a trait by trait basis: Homogeneous Autoregressive (1) (AR(1)), Heterogeneous Autoregressive(1) (ARH(1)), Compound Symmetry (CS), Toeplitz (TOEP), and Unstructured (UN). The first two models also included the random effect of the individual. Model choice was based on evaluation of fit statistics (the (corrected) Akaike's information criterion and the Sawa Bayesian information criterion). Measurements from DXA scans were analyzed with a random mixed model similar to model (1) but excluding the repeated effect of Period and its interactions.

Data are reported as least squares (**LS**) means ± pooled SEM. Differences were considered significant when $P < 0.05$ and a tendency when $0.05 \leq P < 0.10$.

RESULTS

Response to infection

Testing of pooled serum samples and fecal swabs prior to inoculation confirmed the absence of antibodies against both pathogens, as well as no shedding of LI. No mortality occurred and no antimicrobial interventions were required as a result of the dual MhLI challenge. Additionally, pigs showed limited outward symptoms of infectivity during daily observations, with only 2 of the 50 MhLI challenged pigs exhibiting diarrheal symptoms characteristic of LI infections during the entire 6 week period. Serum samples tested over the duration of the experiment confirmed successful inoculation of the pigs in the MhLI challenge group (Fig. 1). Additionally, necropsy of a subset of 24 pigs at dpi 21

confirmed MhLI inoculation via gross lesions and pathogen immunohistochemistry staining for pathogen presence (data not shown). As intended, the status of the Control pigs remained negative over the 6 week challenge period for both LI and Mh antibodies, as well as for LI fecal shedding.

The interaction of dpi x line was not significant for antibody response to either LI or Mh. All MhLI inoculated pigs tested positive for Mh and LI by dpi 14. The Mh antibody response steadily increased over the 6-wk challenge period ($P < 0.01$), whereas the LI antibody response increased until dpi 14 in the LRFI line and until dpi 21 in the HRFI line, after which it began to decline (Fig. 1A and B). LRFI pigs tended to have a higher Mh antibody response than HRFI pigs ($P = 0.06$; Fig. 1A) but there were no differences in antibody response to LI between the lines ($P > 0.05$; Fig. 1B).

The interaction of dpi x line was significant for fecal shedding of LI ($P = 0.009$; Fig. 1C). High RFI pigs excreted higher levels of LI ($P = 0.001$); this was most notable between dpi 14 and 21, when LRFI pigs exhibited a sharp decrease in pathogen shedding, while HRFI pigs continued to shed at a similar level. By week 6 (dpi 42), pigs in both lines no longer had detectable LI in fecal swabs.

Growth performance

Initial body weight differed was 5 kg lower for the LRFI line than for the HRFI line ($P = 0.006$, Table 2), and thus was included as a covariate in model (1) to focus on performance within the challenge period. Repeated measures of changes in BW over the 42 day test period (Fig. 2A) were not affected by MhLI x line x dpi ($P = 0.190$) or Line x dpi ($P = 0.279$). However, irrespective of RFI line, BW changes were significantly lower in MhLI pigs compared to the Control pigs over the entire challenge period ($P < 0.001$). Similarly, there were no line x challenge interactions for ADG, but overall, infection with MhLI decreased ADG by 17% over the 42 day challenge period ($P < 0.001$, Fig. 2B) and MhLI pigs ended the study 3.7 kg lighter than their uninfected Control counterparts ($P = 0.004$, Table 2). Lower ADG in MhLI pigs versus controls was first observed from dpi 8-14. By the end of the 42 day study, MhLI pigs showed recovery and had ADGs similar to the Controls. Although differences in ADG between the lines were not significant ($P > 0.05$), LRFI pigs reached their lowest performance from dpi 22-28, only gaining 0.41 kg/day, after which ADG slowly increased. In contrast, HRFI pigs showed a large drop in ADG from dpi 8-14, after which ADG began to return to that of Controls.

Feed intake was the only growth performance measure that showed a significant line x challenge x dpi interaction ($P = 0.017$), as MhLI pigs consumed significantly less feed than Control pigs, and LRFI pigs consumed less feed than the HRFI group (Fig. 2C). Differences in ADFI between MhLI and Control pigs, with MhLI pigs consuming less feed, were first observed between dpi 8-14. Infected pigs consumed the least feed compared to Controls from dpi 22-28, after which their intake appeared to recover and they consumed at the level of the Controls by the end of 42 days. From dpi 0 to 42, overall ADFI was reduced by 12% in the MhLI pigs versus Controls ($P < 0.001$). As expected based on the selection experiment, LRFI pigs consistently consumed 10-15% less feed than HRFI, regardless of their challenge status throughout the 42 day study ($P < 0.001$).

There was no significant line x challenge interaction for feed efficiency, but in both MhLI and Control pigs, G:F decreased over time ($P < 0.001$; Fig. 2D). Over the entire 42 day challenge, MhLI pigs

demonstrated a 7% reduction in feed efficiency versus Controls ($P < 0.05$). As expected, LRFI pigs had greater feed efficiency ($P < 0.05$) due to their genetic selection to consume less feed for the same ADG.

Whole body composition and tissue accretion

Initial and final body composition and whole body tissue accretion rates are reported in Table 3. There were no significant line x challenge interactions for any of the DXA scan parameters ($P > 0.05$). Initial BW and whole body lean, protein, fat and bone mineral content (**BMC**) mass, and bone mineral density (**BMD**) were not significantly different ($P > 0.05$) between the two challenge groups. There was an initial line effect, as LRFI pigs had more whole body lean and proteinaceous tissue mass ($P < 0.05$), lower fat tissue ($P < 0.05$), and thus tended to have a greater lean to fat ratio ($P = 0.058$).

Final whole body composition shows that the MhLI challenge impacted tissue accretion, regardless of RFI line (Table 3); final BW was 12% lower for the MhLI versus Control pigs ($P = 0.007$), whole body lean and protein mass were 5% lower ($P = 0.001$), BMC was 11% lower ($P = 0.007$), and BMD was 4% lower ($P = 0.022$). Final whole body fat mass did not differ between the MhLI and Control pigs ($P > 0.05$). Genetic selection for RFI affected final body composition, as lean:fat ratio tended to differ, with HRFI pigs exhibiting a lower lean:fat ratio than the LRFI pigs ($P = 0.098$). Bone mineral density was significantly different between lines, with LRFI pigs having greater BMD than HRFI pigs ($P = 0.033$).

Whole body tissue accretion rates over the 47 dpi MhLI challenge period are reported in Table 3. Compared to the controls, MhLI inoculated pigs had 17% lower whole body tissue accretion rate ($P = 0.008$). Other accretion parameters were similarly lower for the MhLI pigs. Lean and protein accretion rates were 17% lower in the MhLI pigs versus Controls ($P = 0.010$), fat accretion rates were 17% lower ($P = 0.013$), and BMC accretion was 15% lower ($P = 0.001$). Line only impacted the accretion rates for BMC, with LRFI pigs tending to have a higher daily accretion ($P = 0.062$).

DISCUSSION

Endemic disease in swine compromises health status, often results in sub-optimal pig performance, and thus leads to economically significant production loss for producers (Schweer et al., 2017; Williams et al., 1997a, b, c). In production systems, pigs often have simultaneous enteric and respiratory challenges. Additionally, there is concern that heavy selection for the economically important trait of feed efficiency results in pigs that are less equipped to overcome pathogen challenge. Therefore, the objective of this paper was to determine if pigs with greater feed efficiency have a greater reduction in growth performance during a dual enteric and respiratory health challenge than pigs with lower feed efficiency. Two lines of pigs divergently selected for RFI were used to model differences in feed efficiency. In previous generations of pigs from these two lines, LRFI pigs consume 0.3 – 0.6 kg less feed per day than HRFI pigs for similar rates of gain, resulting in 10 to 35% greater feed efficiency (Boddicker et al., 2011; Harris et al., 2012; Grubbs et al., 2013). The results herein are consistent with this, as LRFI pigs were 12% more feed efficient than their HRFI counterparts, regardless of challenge status.

The concern that continuous selection for improved feed efficiency results in pigs less equipped to cope with multiple pathogen challenges is based on the hypothesis that pigs selected for high production efficiencies may be genetically pre-programmed to preferentially allocate nutrients to production functions and less able to re-allocate the necessary resources to overcome disease (Rauw et al., 1998; Rauw, 2007). This notion has been somewhat supported by work in poultry, where growing layers of high feed efficiency appeared to be more affected by a *Salmonella enteritidis* infection than layers with low feed efficiency (Van Eerden et al., 2004). In pigs, when divergent RFI lines were challenged with complete Freund's adjuvant, there were no differences in growth or feed intake between the LRFI and HRFI pigs (Merlot et al., 2016), suggesting the two lines coped similarly under immune stress. Further, when subjected to a constant inflammatory challenge with lipopolysaccharide, LRFI and HRFI pigs had similar responses with respect to apparent ileal digestibility, intestinal nutrient transport, and ileal transepithelial resistance (Rakhshandeh et al., 2012). These inflammatory challenges do not truly capture the growth performance impacts that would occur in a pig during an extended disease challenge. In a PRRS disease challenge model, pigs selected for LRFI were actually more robust than HRFI pigs during the challenge, although the difference was small and only significant when analyzed jointly with off-test pigs that were used as a control group (Dunkelberger et al., 2015). Additionally, the tendency for high FE pigs to be more robust in response to infection were primarily based on faster, heightened antibody responses and decreased viral load, rather than growth performance (Dunkelberger et al., 2015). Although the HRFI and LRFI pigs utilized in the study herein had strikingly different patterns of LI fecal shedding, bacterial fecal shedding only loosely correlates with the presence of clinical disease, and should be interpreted simply as a diagnostic tool rather than as a tool to make comparisons about disease severity (Burrough et al., 2015). The performance data, a more economically relevant measure of disease severity than diagnostic methods, in the study herein suggest that selection for low RFI, or high FE, does not affect the changes in ADG, G:F, or whole body tissue accretion that result from a MhLI challenge.

Enteric pathogens compromise the functionality of the gastrointestinal tract through a variety of mechanisms. *Lawsonia intracellularis* invades the immature enterocytes of the intestinal crypts and stimulates mitosis, while inhibiting normal epithelial cell differentiation (Moeser and Blikslager, 2007). Reductions in weight gain and feed efficiency attributed to LI infections are thought to be a result of lost body protein and amino acids into the intestinal lumen in combination with reduced nutrient absorption, as newly formed enterocytes are unable to reach their normal absorptive capacity (McOrist and Gebhart, 2012). In a typical LI challenge model, bacteria can be found in the intestines and feces 1-3 weeks post inoculation, with peak clinical symptoms and lesions occurring 3 weeks following inoculation (McOrist and Gebhart, 2012). *Lawsonia intracellularis* manifests clinically with considerable variation, but symptoms include lethargy, anorexia, diarrhea, and even sudden death from a hemorrhagic form of proliferative enteropathy, depending on stage of production, pre-existing immune status, and severity of infection. Experimental inoculation with LI consistently reduces ADG by 6-20% and feed efficiency by 6-25% (Gogolewski et al., 1991; McOrist et al., 1996; McOrist et al., 1997; Paradis et al., 2012). Subclinical proliferative enteropathy still causes hyperplasia, decreased absorptive capacity, and reduced performance without outward symptoms of illness, making diagnosis and treatment in a large-scale setting difficult (McOrist and Gebhart, 2012; Paradis et al., 2012). In a subclinical LI challenge

model in nursery pigs that displayed limited outward signs of disease, Paradis et al. (2012) found ADG and feed efficiency reductions of 37 and 27%, respectively. The reductions in performance parameters in the present study as a result of MhLI inoculation, while significant, were not as marked as those observed by Paradis et al. (2012), but the grow-finish pigs utilized herein were older than those often utilized in inoculation models. Additionally, pigs were evaluated over 6 weeks, a time period long enough to allow recovery from infection.

Pigs under inflammatory stress, as observed during Mh infection, show reductions in feed intake due to cytokines such as interleukin (**IL**)-1β, IL-6, and tumor necrosis factor (**TNF**) α (Escobar et al., 2002; Thacker and Minion, 2012). Consequences of decreased feed intake include decreased BW gain and protein accretion. However, Escobar et al. (2002; 2004) reported no differences in feed intake, ADG, or feed efficiency in two separate 28 day Mh studies using nursery pigs, despite increased mRNA abundance of IL-1β, IL-6, and TNF-α in the lungs of infected pigs, while pigs infected with PRRS and a Mh/PRRS combination exhibited marked reductions in ADG. However, these experiments were performed in disease containment chambers that prevented potentiation with any other pathogens or immunological stressors. Under less controlled conditions, results show varied decreases in ADG and ADFI but limited impacts on feed efficiency (Straw, 1991; Clark et al., 1993; Scheidt et al., 1994; Ciprian et al., 2012). However, severe enzootic pneumonia resulting from Mh and *Pasteurella multocida* co-infection has been demonstrated to have marked impacts on pig ADG, ADFI, and G:F (Eamens et al. 2007; Wyburn et al. 2011). Additionally, Mh co-infection with *Pasteurella multocida* increases lesion severity, and decreases carcass fat percentage as measured via computed tomography compared to pigs infected with Mh alone (Eamens et al. 2007). In the current study, it is not possible to elucidate disease-specific impacts, but reduced feed intake resulting from pulmonary inflammation is a likely cause of decreased performance. Therefore, the reductions in ADG, GF, as well as lean tissue accretion observed herein are likely due to a combination of feed intake reduction from both Mh and LI challenge, plus an additional loss of nutrients due to decreased absorption from the enterocytes due to LI infection. These reductions in performance are especially interesting considering MhLI pigs maintained a relatively healthy appearance throughout the experiment, with limited clinical symptoms of either pathogen.

Measuring longitudinal tissue accretion allows examination of the tissue components that are most affected under a health challenge, and how growth is repartitioned under immune stress. Our group has previously reported that feed efficiency and whole body protein accretion rates are profoundly impacted by controlled pathogen challenge (i.e. PRRS infection) in grow-finisher pigs (Schweer et al., 2017). However, to the knowledge of the authors, this is the first study in which longitudinal tissue accretion has been reported for this particular pathogen combination and for LI infection in general. Longitudinal tissue accretion during Mh infection was reported by Escobar et al. (2002; 2004), who examined tissue accretion via serial slaughter in pigs experimentally infected with Mh alone and with a Mh/PRRSV combination, with housing in disease containment chambers. In both cases, Mh alone caused no differences in protein, lipid and ash accretion, while PRRS reduced protein accretion by over 50% (Escobar et al., 2002; 2004). Although the present study is unable to elucidate disease specific effects, it is likely that both Mh and LI were responsible for the observed reductions in tissue accretion. Infected pigs showed similar reductions in lean, protein, fat, and BMC accretion (16, 16, 16,

and 15%, respectively). Similar reductions in all tissues would indicate that the differences are due to an overall slower rate of gain, and that growth is not repartitioned during this health challenge.

Genetic selection for residual feed intake, although not impacting response to pathogen challenge, did impact body composition. Total fat was lower in the highly efficient pigs at both DXA time points. This is consistent with previous results for these selection lines, describing both decreased backfat and lower percentage of fat in market weight pigs in the LRFI versus HRFI lines (Cai et al., 2008; Boddicker et al., 2011; Smith et al., 2011).

In conclusion, the results presented herein demonstrate that selection for RFI alters the body composition of grow-finish pigs, but genetic selection for enhanced feed efficiency does not disadvantage pigs during an extended health challenge. However, a dual respiratory and enteric challenge does decrease growth, feed efficiency and tissue accretion of grow-finish pigs over a 42 day experimental challenge period, regardless of genetic line. This study also presents evidence that a mild pathogen load, with no mortality or necessity for antimicrobial intervention, still significantly impairs growth performance, indicating a need to further characterize the full impact of subclinical infections on growing pigs.

LITERATURE CITED

Boddicker, N., N. K. Gabler, M. E. Spurlock, D. Nettleton, and J. C. M. Dekkers. 2011. Effects of ad libitum and restricted feeding on early production performance and body composition of Yorkshire pigs selected for reduced residual feed intake. J. Anim. Sci. 5: 1344-1353. doi:10.1017/S175173111100036X.

Brandt, D., U. Kaim, W. Baumgartner, and M. Wendt. 2010. Evaluation of Lawsonia intracellularis infection in a group of pigs in a subclinically affected herd from weaning to slaughter. Vet. Microbiol. 146: 361-365. doi:10.1016/j.vetmic.2010.05.021.

Burrough, E. R., M. L. Rotolo, P. C. Gauger, D. M. Madson, and K. J. Schwartz. 2015. Correlation of Lawsonia intracellularis semi-quantitative fecal polymerase chain reaction assay results with the presence of histologic lesions of proliferative enteropathy and positive immunohistochemical staining. JSHAP 23: 204-207.

Cai, W., D. S. Casey, and J. C. M. Dekkers. 2008. Selection response and genetic parameters for residual feed intake in Yorkshire swine. J. Anim. Sci. 86: 287-298. doi:10.2527/jas.2007-0396.

Ciprian, A., J. M. Palacios, D. Quintanar, L. Batista, G. Colmenares, T. Cruz, A. Romero, W. Schnitzlein, and S. Mendoza. 2012. Florfenicol feed supplemented decrease the clinical effects of Mycoplasma hyopneumoniae experimental infection in swine in Mexico. Res. Vet. Sci. 92: 191-196. doi:10.1016/j.rvsc.2011.01.010.

Clark, L. K., C. H. Armstrong, and A. B. Scheidt. 1993. The effect of Mycoplasma hyopneumoniae infection on growth in pigs with or without environmental constraints. JSHAP 1: 10-14.

Colpoys, J. D., A. K. Johnson, and N. K. Gabler. 2016. Daily feeding regimen impacts pig growth and behavior. Physiol. Behav. 159: 27-32. doi:10.1016/j.physbeh.2016.03.003.

Curry, S. M., K. A. Gibson, E. R. Burrough, K. J. Schwartz, K. J. Yoon, and N. K. Gabler. 2017. Nursery pig growth performance and tissue accretion modulation due to porcine epidemic diarrhea virus or porcine deltacoronavirus challenge. J. Anim. Sci. 95: 173-181. doi:10.2527/jas.2016.1000.

Dunkelberger, J. R., N. J. Boddicker, N. V. L. Serao, J. M. Young, R. R. R. Rowland, and J. C. M. Dekkers. 2015. Response of pigs divergently selected for residual feed intake to experimental infection with the PRRS virus. Livest. Sci. 177: 132-141. doi:10.1016/j.livsci.2015.04.014.

Eamens, G. J., K. J. James, I. M. Barchia, and L. R. Giles. 2007. Use of computed tomography in live pigs to measure the impact of pneumonia on carcass composition. In: Australasian pig science association manipulating pig production. p 60.

Escobar, J., W. G. Van Alstine, D. H. Baker, and R. W. Johnson. 2002. Growth performance and whole-body composition of pigs experimentally infected with Mycoplasma hyopneumoniae. J. Anim. Sci. 80: 384-391.

Escobar, J., W. G. Van Alstine, D. H. Baker, and R. W. Johnson. 2004. Decreased protein accretion in pigs with viral and bacterial pneumonia is associated with increased myostatin expression in muscle. J. Nutr. 134: 3047-3053.

Gogolewski, R. P., R. W. Cook, and E. S. Batterham. 1991. Suboptimal growth associated with porcine intestinal adenomatosis in pigs in nutritional studies. Aust. Vet. J. 68: 406-408. doi:10.1111/j.1751-0813.1991.tb03114.x.

Grubbs, J. K., A. N. Fritchen, E. Huff-Lonergan, J. C. M. Dekkers, N. K. Gabler, and S. M. Lonergan. 2013. Divergent genetic selection for residual feed intake impacts mitochondria reactive oxygen species production in pigs. J. Anim. Sci. 91: 2133-2140. doi:10.2527/jas.2012-5894.

Harris, A. J., J. F. Patience, S. M. Lonergan, J. M. D. C, and N. K. Gabler. 2012. Improved nutrient digestibility and retention partially explains feed efficiency gains in pigs selected for low residual feed intake. J. Anim. Sci. 90 Suppl 4: 164-166. doi:10.2527/jas.53855.

Johnson, R. W. 2012. Fueling the immune response: What's the cost? In: J. F. Patience (ed.) Feed efficiency in swine. p 211-223. Wageningen Academic Publishers.

Labussière, E., S. Dubois, H. Gilbert, J. N. Thibault, N. Le Floc'h, J. Noblet, and J. van Milgen. 2015. Effect of inflammation stimulation on energy and nutrient utilization in piglets selected for low and high residual feed intake. J. Anim. Sci. 9: 1653-1661. doi:10.1017/S1751731115000932.

McOrist, S., and C. J. Gebhart. 2012. Proliferative enteropathy. In: J. J. Zimmerman, L. A. Karriker, A. Ramirez, K. J. Schwartz and G. W. Stevenson (eds.) Diseases of Swine. p 811-820. Wiley-Blackwell, West Sussex.

McOrist, S., S. H. Smith, and L. E. Green. 1997. Estimate of direct financial losses due to porcine proliferative enteropathy. Vet. Rec. 140: 579-581.

McOrist, S., S. H. Smith, M. F. Shearn, M. M. Carr, and D. J. Miller. 1996. Treatment and prevention of porcine proliferative enteropathy with oral tiamulin. Vet. Rec. 139: 615-618.

Merlot, E., H. Gilbert, and N. Le Floc'h. 2016. Metabolic response to an inflammatory challenge in pigs divergently selected for residual feed intake. J. Anim. Sci. 94: 563-573. doi:10.2527/jas.2015-9445.

Moeser, A. J., and A. T. Blikslager. 2007. Mechanisms of porcine diarrheal disease. J. Am. Vet. Med. Assoc. 231: 56-67. doi:10.2460/javma.231.1.56.

National Research Council. 2012. Nutrient requirements of swine: Eleventh revised edition. The National Academies Press, Washington, DC.

Paradis, M. A., C. J. Gebhart, D. Toole, G. Vessie, N. L. Winkelman, S. A. Bauer, J. B. Wilson, and C. A. McClure. 2012. Subclinical ileitis: Diagnostic and performance parameters in a multi-dose mucosal homogenate challenge model. JSHAP 20: 137-142.

Rakhshandeh, A., J. C. M. Dekkers, B. J. Kerr, T. E. Weber, J. English, and N. K. Gabler. 2012. Effect of immune system stimulation and divergent selection for residual feed intake on digestive capacity of the small intestine in growing pigs. J. Anim. Sci. 90: 233-235. doi:10.2527/jas.53976.

Rauw, W. 2007. Physiological consequences of selection for increased performance. In: Proc. Assoc. Advmt. Anim. Breed. Genet. p 240-247.

Rauw, W. M., E. Kanis, E. N. Noordhuizen-Stassen, and F. J. Grommers. 1998. Undesirable side effects of selection for high production efficiency in farm animals: A review. Livest. Prod. Sci. 56: 15-33. doi:Doi 10.1016/S0301-6226(98)00147-X.

Scheidt, A. B., V. B. Mayrose, and A. W. G. Van. 1994. The effects of vaccinating pigs for mycoplasmal pneumonia in a swine herd affected by enzootic pneumonia. JSHAP 2: 7-11.

Schweer, W. P., K. Schwartz, J. F. Patience, L. Karriker, C. Sparks, M. Weaver, M. Fitzsimmons, T. E. Burkey and N. K. Gabler. 2017. Porcine Reproductive and Respiratory Syndrome virus reduces feed efficiency, digestibility and lean tissue accretion in grow-finish pigs. Transl. Anim. Sci. *Accepted In Press*.

Sibila, M., M. Pieters, T. Molitor, D. Maes, F. Haesebrouck, and J. Segales. 2009. Current perspectives on the diagnosis and epidemiology of Mycoplasma hyopneumoniae infection. Vet. J. 181: 221-231. doi:10.1016/j.tvjl.2008.02.020.

Smith, R. M., N. K. Gabler, J. M. Young, W. Cai, N. J. Boddicker, M. J. Anderson, E. Huff-Lonergan, J. C. M. Dekkers, and S. M. Lonergan. 2011. Effects of selection for decreased residual feed intake on composition and quality of fresh pork. J. Anim. Sci. 89: 192-200. doi:10.2527/jas.2010-2861.

Straw, B. E. 1991. Performance measured in pigs with pneumonia and housed in different environments. J. Am. Vet. Med. Assoc. 198: 627-630.

Suster, D., B. J. Leury, E. Ostrowska, K. L. Butler, D. J. Kerton, J. D. Wark, and F. R. Dunshea. 2003. Accuracy of dual energy X-ray absorptiometry (DXA), weight and P2 back fat to predict whole body and carcass composition in pigs within and across experiments. Livest. Prod. Sci. 84: 231-242. doi:10.1016/S0301-6226(03)00077-0.

Thacker, E. L., and C. F. Minion. 2012. Mycoplasmosis. In: J. J. Zimmerman, L. A. Karriker, A. Ramirez, K. J. Schwartz and G. W. Stevenson (eds.) Diseases of Swine. p 779-797. Wiley-Blackwell, West Sussex.

Van Eerden, E., H. Van den Brand, G. De Vries Reilingh, H. K. Parmentier, M. C. M. de Jong, and B. Kemp. 2004. Residual feed intake and its effect on Salmonella enteritidis infection in growing layer hens. Poult. Sci. 83: 1904-1910. doi:10.1093/ps/83.11.1904.

Williams, N. H., T. S. Stahly, and D. R. Zimmerman. 1997a. Effect of chronic immune system activation on body nitrogen retention, partial efficiency of lysine utilization, and lysine needs of pigs. J. Anim. Sci. 75: 2472-2480. doi:10.2527/1997.7592472x.

Williams, N. H., T. S. Stahly, and D. R. Zimmerman. 1997b. Effect of chronic immune system activation on the rate, efficiency, and composition of growth and lysine needs of pigs fed from 6 to 27 kg. J. Anim. Sci. 75: 2463-2471. doi:10.2527/1997.7592463x.

Williams, N. H., T. S. Stahly, and D. R. Zimmerman. 1997c. Effect of level of chronic immune system activation on the growth and dietary lysine needs of pigs fed from 6 to 112 kg. J. Anim. Sci. 75: 2481-2496. doi:10.2527/1997.7592481x.

Wyburn, G. L., G. J. Eamens, D. Collins, and A. M. Collins. 2015. Rapid changes occur in feed efficiency after infection with *Mycoplasma hyopneumoniae* and *Pasteurella multocida*. Animal Production Science 55: 1568-1568. doi:https://doi.org/10.1071/ANv55n12Ab027

Table 1. Diet composition, as fed

Ingredient	%
Corn	66.67
Soybean meal	8.40
Corn DDGS[1]	22.50
Soybean Oil	0.51
Lysine	0.25
Salt	1.03
Vitamin-mineral premix[2]	0.13
Phytase[3]	0.01
Calculated composition	
ME, kcal/kg	3,400
Crude Protein, %	15.5
SID Lysine, %	0.87
STTD P, %	0.28

[1]DDGS = dried distiller's grains with solubles

[2]Vitamin-mineral premix supplied (per kg of diet): 66,000,000 IU vitamin A, 12,120,000 IU vitamin D3, 35,200 IU vitamin E, 0.022 g vitamin B, 3.3 g riboflavin, 13.2 g D-pantothenic acid, 16.61 g niacin, 1.496 g ethoxyquin, 0.6 g I as ethylenediamine dihydroiodide, 0.133 g Se as sodium selenite, 1.6 g Cu as copper chloride, 4 g Mn as manganous oxide, 88 g Zn as zinc oxide, and 88 g Fe as ferrous carbonate and ferrous sulfate.

[3]Phytase supplied as Ronozyme NP (DSM, Heerlen, Netherlands) containing 10,000 FYT/g of product for a final activity of 1, 000 FYT/kg diet

Table 2. Weekly performance parameters of low (LRFI) or high (HRFI) residual feed intake pigs in control and *Mycoplasma hyopneumoniae + Lawsonia intracellularis* (MhLI) challenge groups from days post inoculation (dpi) 0-42.

Item	Treatment				SEM	*P*-value[3]						
	LRFI-Control	HRFI-Control	LRFI-MhLI	HRFI-MhLI		MhLI	Line	dpi	MhLI x dpi	Line x dpi	MhLI x Line	MhLI x Line x dpi
Pre-challenge period (dpi -21 to dpi 0)												
ADG, kg/d[1]	0.85	0.89	0.85	0.88	0.030	0.990	0.302	-	-	-	0.861	-
ADFI, kg/d[1]	2.18[a]	2.54[b]	2.09[a]	2.63[b]	0.075	0.913	<0.001	-	-	-	0.040	-
G:F[1]	0.43[a]	0.30[b]	0.41[a]	0.34[b]	0.046	0.743	0.020	-	-	-	0.389	-
Challenge period												
Start BW, kg[1]	64.8[a]	71.4[b]	63.0[a]	72.1[b]	1.929	0.588	0.006	-	-	-	0.189	-
End BW, kg[2]	102.7[ab]	104.1[a]	99.1[c]	100.3[bc]	1.268	0.004	0.337	-	-	-	0.940	-
ADG, kg/d												
dpi 0 – 7[1]	0.90	0.89	0.84	0.84	0.051	<0.001	0.263	<0.001	<0.001	0.382	0.907	0.113
dpi 8 – 14[1]	0.86	0.91	0.69	0.56	0.053							
dpi 15 – 21[1]	0.81	0.81	0.59	0.67	0.082							
dpi 22 – 28[2]	0.68	0.64	0.41	0.55	0.064							
dpi 29 – 35[2]	0.70	0.78	0.49	0.65	0.052							
dpi 35 – 42[2]	0.51	0.62	0.68	0.63	0.049							
ADFI, kg/d												
dpi 0 – 7[1]	2.44	2.75	2.25	2.74	0.083	<0.001	<0.001	<0.001	<0.001	0.185	0.375	0.031

dpi 8 – 14[1]	2.57	3.02	2.32	2.52	0.090							
dpi 15 – 21[1]	2.81	3.31	2.08	2.45	0.121							
dpi 22 – 28[2]	2.54	2.95	2.02	2.42	0.101							
dpi 29 – 35[2]	2.52	3.08	2.25	2.81	0.095							
dpi 35 – 42[2]	2.47	3.19	2.60	3.01	0.120							
G:F												
dpi 0 – 7[1]	0.37	0.35	0.36	0.31	0.014	0.001	0.035	<0.001	<0.001	0.370	0.759	0.140
dpi 8 – 14[1]	0.34	0.30	0.30	0.21	0.021							
dpi 15 – 21[1]	0.29	0.26	0.20	0.20	0.039							
dpi 22 – 28 [2]	0.27	0.22	0.19	0.22	0.028							
dpi 29 – 35 [2]	0.28	0.25	0.21	0.23	0.018							
dpi 35 – 42 [2]	0.21	0.19	0.26	0.21	0.014							

[a,b,c]Means with differing subscripts indicate a significant (P<0.05) difference.

[1]25 barrows/line/challenge

[2]19 barrows/line/challenge

[3]Challenge period performance P-values from repeated measures analysis encompassing dpi 0-42.

Table 3. Whole body composition and tissue accretion rates of low (LRFI) and high (HRFI) residual feed intake barrows dual challenged with or without *Mycoplasma hyopneumoniae and Lawsonia intracellularis* (MhLI)[1]

Item	Treatment				SEM	*P*-value		
	LRFI-Control	HRFI-Control	LRFI-MhLI	HRFI-MhLI		MhLI	Line	MhLI x Line
Initial composition								
BW, kg	70.33	74.06	71.44	74.11	2.202	0.641	0.298	0.674
Lean, kg	57.14	57.76	55.44	56.94	1.873	0.274	0.676	0.700
Protein, kg	11.18	11.31	10.83	11.14	0.387	0.274	0.675	0.700
Fat, kg	10.92^{a}	12.59^{bc}	11.43^{ac}	13.28^{b}	0.547	0.165	0.025	0.830
Lean:Fat	5.34^{a}	4.73^{ab}	5.00^{ab}	4.34^{b}	0.233	0.071	0.042	0.885
BMC[2] , kg	1.96	2.08	1.98	2.03	0.071	0.754	0.338	0.547
BMD[3], g/cm^3	0.87	0.89	0.86	0.89	0.013	0.722	0.081	0.489
Final composition								
BW, kg	110.14^{ab}	115.37^{a}	102.68^{b}	108.24^{ab}	3.939	0.026	0.294	0.957
Lean, kg	83.68^{a}	84.60^{a}	77.41^{b}	79.30^{b}	2.894	0.022	0.698	0.830
Protein, kg	16.67^{a}	16.86^{a}	15.38^{b}	15.77^{b}	0.598	0.022	0.698	0.830
Fat, kg	20.22	23.88	19.40	22.47	1.294	0.233	0.064	0.742
Lean:Fat	4.24	3.68	4.17	3.62	0.228	0.742	0.068	0.991
BMC , kg	3.51^{a}	3.44^{ab}	3.24^{ab}	3.24^{ab}	0.092	0.019	0.709	0.649

BMD, g/cm^3	1.13^a	1.08^{ab}	1.08^{ab}	1.04^b	0.016	0.013	0.034	0.622
Whole body accretion, g/d								
Total body	789.7^a	842.1^a	660.3^{ab}	697.6^b	48.01	0.008	0.422	0.863
Lean	541.6^a	547.8^a	448.4^b	456.5^{ab}	30.76	0.010	0.829	0.975
Protein	112.0^a	113.3^a	92.7^b	94.4^{ab}	6.36	0.010	0.829	0.975
Fat	189.7^{ab}	230.4^a	162.7^b	187.7^b	17.57	0.013	0.168	0.524
BMC	31.7^a	27.6^b	25.8^b	24.8^b	1.08	0.001	0.065	0.130

^{a,b,c} Means with differing superscripts indicate a significant ($P < 0.05$) difference.

[1]Initial composition was performed at -2 days post inoculation (dpi) and final composition at dpi 47. Whole body composition was determined by dual x-ray absorptiometry (DXA) scans (7 barrows/line/challenge).

[2]BMC = bone mineral content

[3]BMD = bone mineral density

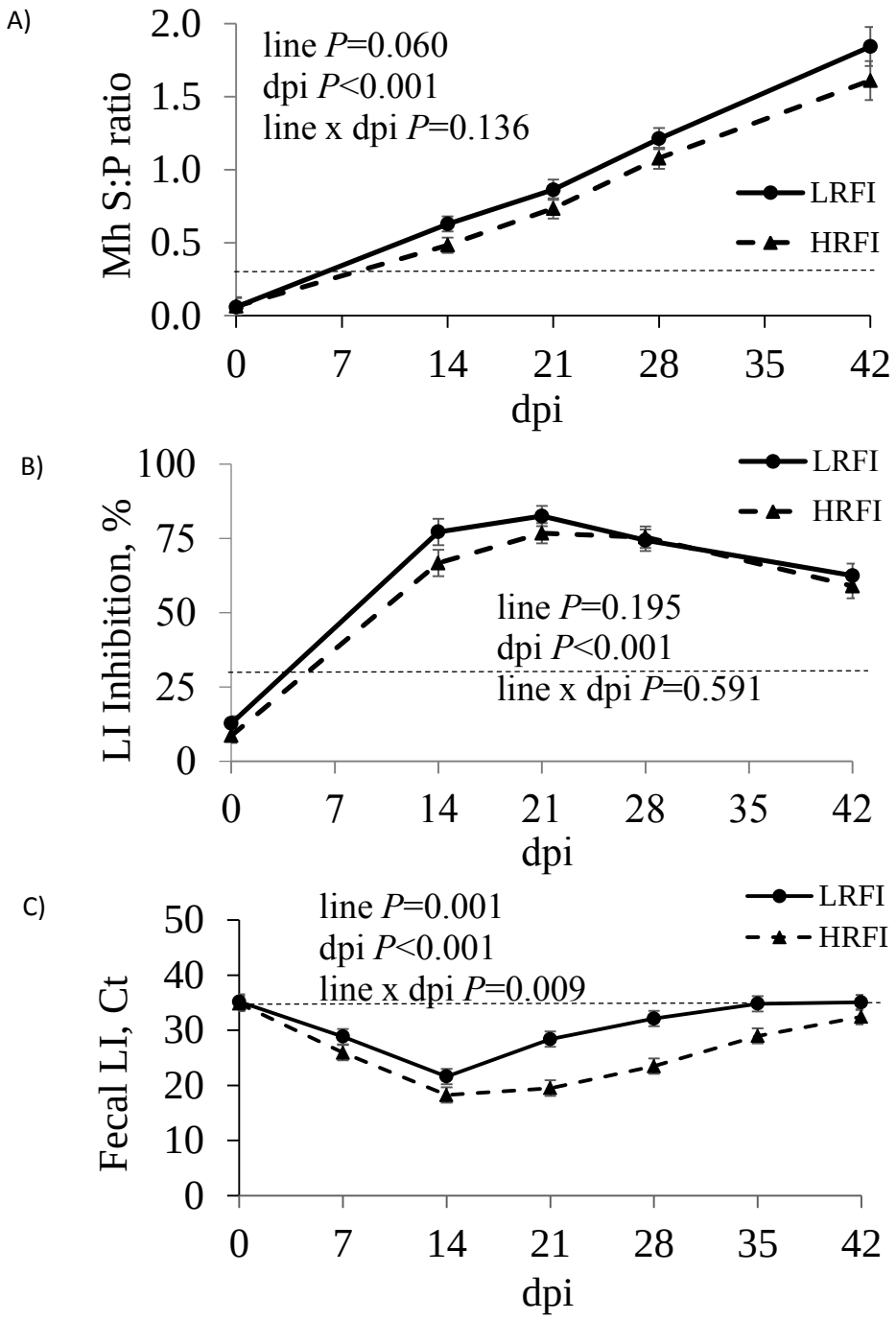

Figure 1. Serology and fecal shedding response of low (LRFI) and high (HRFI) residual feed intake barrows dual inoculated with *Mycoplasma hyopneumoniae* and *Lawsonia intracellularis* (MhLI). **A)** Serum antibody titers to *Mycoplasma hyopneumoniae* (Mh, 25 barrows/line) in which an S:P between 0.3-0.40 is suspect and an S:P > 0.4 is positive for Mh, **B)** Serum antibody titers to *Lawsonia intracellularis* (LI, 25 barrows/line) in which % inhibition between 20-30% is suspect and % inhibition > 30 is positive for LI, and **C)** Fecal shedding of LI (7 barrows/line) in which a PCR cycle-threshold (**Ct**) value <35 is considered positive for LI presence and Ct >35 is interpreted as negative.

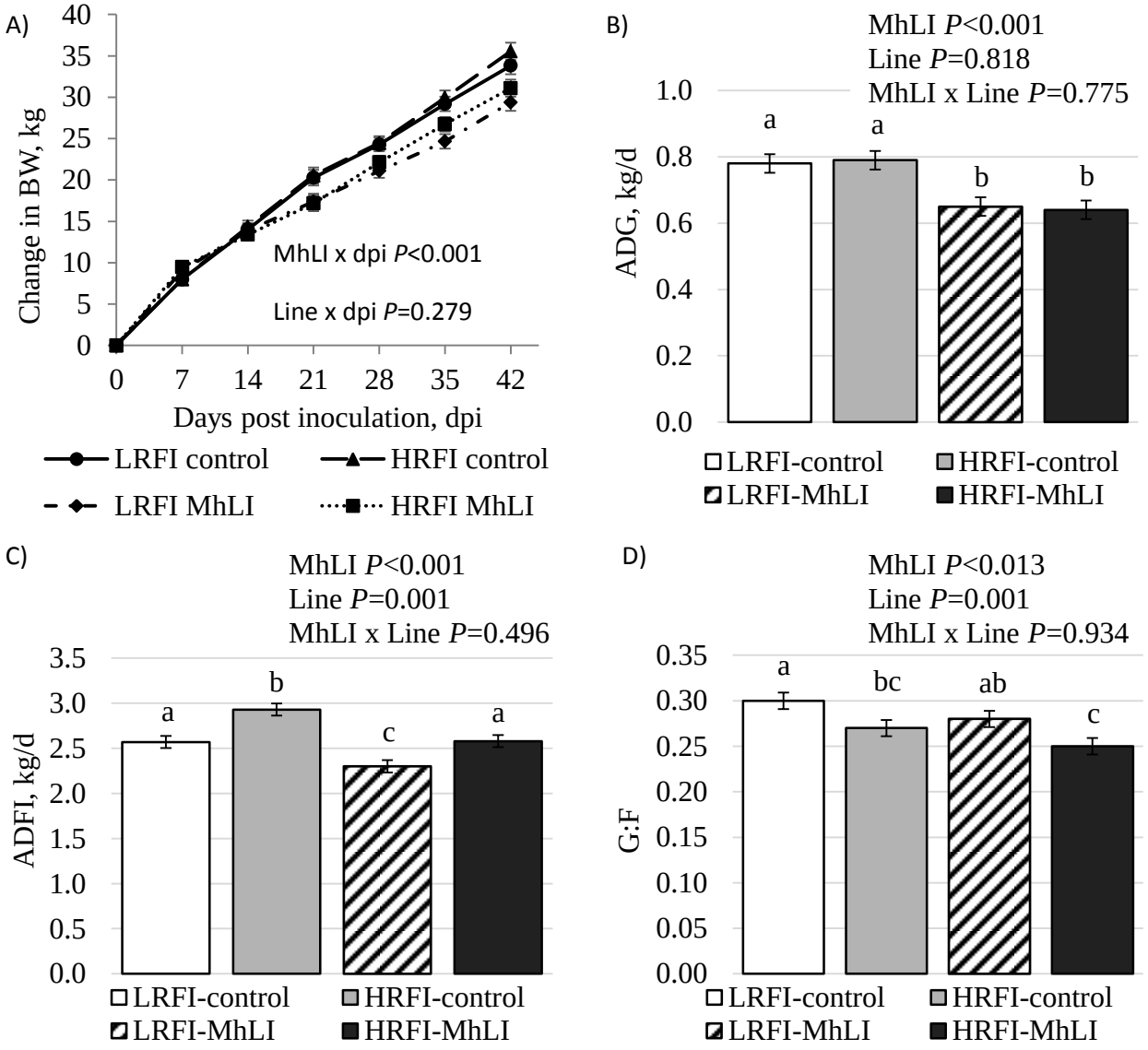

Figure 2. Effect of dual *Mycoplasma hyopneumonia* + *Lawsonia intracellularis* challenge (MhLI) on overall performance of pigs divergently selected for low (LRFI) or high (HRFI) residual feed intake (Line). **A)** BW gains, **B)** ADG, **C)** ADFI, and **D)** G:F over the entire challenge period (*n* = 25 barrows/line/challenge). Pigs were inoculated with both pathogens on days post inoculation (dpi) 0 and parameters were assessed weekly for 42 days post infection.