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ASSOCIATION BETWEEN ENDOMETRITIS AND UROCYSTITIS IN CULLED SOWS

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Slaughterhouse sampling and examination of urogenital tracts of 499 sows and gilts culled for reproductive reasons from 21 Hungarian herds were performed over a 6-year period. The aim was to estimate the prevalence of different urogenital tract lesions, and to provide sensitivity and specificity estimates for macroscopic and bacteriological examinations in the diagnosis of urocystitis and endometritis. Furthermore, the association between endometritis and urocystitis was assessed. The prevalence of main lesions of the urogenital tract was similar to that reported in other studies. The 'sensitivity' of macroscopic and bacteriological methods was determined statistically by taking histopathology as the 'Gold Standard'. As a result, the 'sensitivity' of macroscopic methods for the diagnosis of endometritis and urocystitis was ≤ 18.1% and 47.9%, respectively, while the 'sensitivity' of bacteriology for the diagnosis of the same conditions was ≤ 31.8% and 63.0%, respectively. The presumed positive association between urocystitis and endometritis was confirmed; it was not confounded by parity. Animals affected by urocystitis had a 3.5 times higher odds to simultaneously have endometritis than animals without urocystitis.

Key words: Swine, endometritis, urocystitis

Slaughterhouse sampling and subsequent examination of female reproductive organs is a valuable tool in swine reproductive management. Examination of reproductive organs of sows and gilts culled for infertility provides useful data on the possible causes of reproductive failure (Straw et al., 1986; Almond and Richards, 1992; Tubbs, 1995; Ványi et al., 1995; Dalin et al., 1997; Heinonen et al., 1998). Such examinations are considered particularly useful in the case of non-infectious reproductive problems and urogenital tract diseases, where serological and epidemiological investigations are of limited value.

A slaughtercheck is usually a 'one-time' examination of a herd problem. Statistical drawbacks of this approach are discussed in the literature (Martin et al., 1987; Almond and Richards, 1992). Examining a large number of culled

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sows from several farms over a longer period of time can provide more information on the prevalence of reproductive-tract lesions and can help to reveal cause-effect relationships and seasonal fluctuations (Geudeke et al., 1992). Results of reproductive slaughterchecks (Almond and Richards, 1992; Dee, 1992; Tubbs, 1995) have to be evaluated together with detailed production data pertaining to the reproductive performance of individual breeding animals.

Diagnosis of endometritis and/or urocystitis was based on macroscopic and/or bacteriological examinations by several authors (Möller et al., 1981; Geudeke et al., 1992); however, the sensitivity and specificity of these methods are often not optimal. Although endometritis and urocystitis frequently occur concurrently (Meredith, 1986; Dee, 1992; Madec and Leon, 1992), their association is not confirmed by statistical analyses in several reports (Möller et al., 1981; Thornton et al., 1998). Moreover, data on the magnitude of their association are not reported in the literature. It has been postulated that higher parity predisposes to both endometritis and urocystitis (Dial and MacLachlan, 1988; Dee, 1992). In this case, parity may confound the urocystitis-endometritis association (Martin et al., 1987; Thrusfield, 1995).

In this study, the prevalence of different reproductive-tract lesions found at swine reproductive slaughterchecks in Hungary was estimated. Furthermore, the sensitivity and specificity of macroscopic and/or bacteriological examinations in the diagnosis of endometritis and urocystitis were assessed. The association between these two conditions accounting for the possible confounding effect of parity was also assessed, using Mantel-Haenszel analysis.

Materials and methods

Examinations on the reproductive organs of culled sows and gilts collected at slaughter were performed over a 6-year period (1995–2000). Farms were enrolled in this study upon request for reproductive examination. Twenty-one large swine herds from the main pig-producing regions of Hungary were included. Some farms were sampled several times during the study period. Sow herd size ranged from 300 to 2000 (median: 750). A total of 499 sows were examined (range 4–53/farm). Out of this sample, due to loss or unavailability, data from only 353 animals (range 1–49/farm) were analysed.

Animals and herd characteristics

Animals were selected for culling for reproductive failure by farm managers. Investigators had no influence on animal selection, selection was not made at random. Only animals with clearly indicated reproductive failure in their records were included in the study. Inclusion criteria were: multiple regular or irregular repeats with or without vaginal discharge, anoestrus, and ‘failure to farrow’. For

each animal parity, reason for culling, and the interval from last weaning or breeding to slaughter were obtained. Due to the lack of computerised herd record system on most farms, data were mainly obtained from hand-written sow registration cards. It was not possible to check herd records for errors; however, in case of any doubt about validity, records of the sow were not processed.

Slaughterhouse sampling

The method of slaughterhouse sample collection was similar to that described by several authors (Straw, 1986; Almond and Richards, 1992; Tubbs, 1995). Briefly, approx. 90% of the samples were taken at the same large commercial slaughterhouse with an approximate line speed of 200 sows/hour. The rest of the samples were collected from smaller slaughterhouses. Sows were identified by their ear-tags at two separate places in the slaughter line. Whole reproductive tracts (ovaries, oviducts, uterine horns and body, cervix, vagina, vestibule and vulva) and the urinary bladder with the urethra were collected from the viscera trays into clean plastic boxes. Kidneys and ureters were not examined, because their safe collection was prevented by the high line speed. The neck of the bladder and the vagina were tied with a string to lessen their bacterial contamination during transport. Samples were then transferred to clean plastic bags, and were transported to our laboratory in cooling boxes.

Macroscopic examinations

All urogenital tracts were completely dissected after collecting samples for bacteriology. Lesions were described by the same person in all cases; findings were recorded on microcassette tape. Ovaries were measured, their surface structures were counted, measured and described to determine the stage of sexual cycle and to diagnose ovarian abnormalities (Schnurrbusch et al., 1985; Leiser et al., 1988; Almond and Richards, 1992). Integrity and content of the oviducts were recorded. Diameter and content of uterine horns (amount, physical characteristics, odour), and the state of endometrium (surface integrity, fluid content, vascularisation) were checked. Endometritis was diagnosed macroscopically when any thick, purulent material, or thin, turbid fluid without developmental anomaly of the tubular genital tract was present in the lumen of at least one of the horns. Content of the bladder, thickness of its wall, and the state of the urothelium (integrity, fluid content and vascularization) were recorded. Urocystitis was diagnosed macroscopically upon the following lesions: (1) at least moderate diffuse congestion of the urothelium, or (2) substantial thickening of the wall or (3) presence of mucosal oedema and haemorrhages, or (4) presence of purulent material or fibrin flecks in the lumen. The presence of concretions in the bladder was also noted, but it did not indicate urocystitis in itself. All visible developmental anomalies of the available urogenital tract and the presence of pregnancy also were noted.

Histopathology

Full-thickness samples (about 4 × 1 cm) from the mid-portion of both uterine horns, and from the fundus of the bladder were cut and fixed in 8% formaldehyde solution for histopathological examinations. Samples subsequently were embedded in paraffin, cut at 6 μm, stained with haematoxylin-eosin (H.-E.) and were examined for the presence of inflammatory lesions under light microscope by the same person. The examiner was unaware of the history, macroscopic and bacteriological test results of animals from which histological samples were originated. Only one section from each mentioned sampling place was evaluated, sections were evaluated in their entirety.

Stage of reproductive cycle in each animal was estimated using guidelines from the literature (Schnurrbusch et al., 1985; Leiser et al., 1988). If the histological appearance of the endometrium did not compare with the state of ovaries, sows were excluded from further analyses in order to prevent possible misdiagnoses related to oestrogenic mycotoxicoses (Ványi et al., 1995; Glávits and Ványi, 1995).

Endometritis was diagnosed histopathologically, (1) when the endometrium contained large number [> 5/high-power field (400 ×, HPF)] of neutrophil granulocytes, lymphocytes and/or plasma cells in the epithelium and stratum compactum; (2) when there was more than one focal periglandular or perivascular inflammatory cell accumulation in the stratum spongiosum; or (3) when diffuse leukocytic infiltration of the stratum spongiosum was observed (Figs 1 and 2). Urocystitis was diagnosed when the mucosa contained more than one inflammatory focus subepithelially or in the propria, or more than 5 inflammatory cells/HPF were seen (Figs 3 and 4).

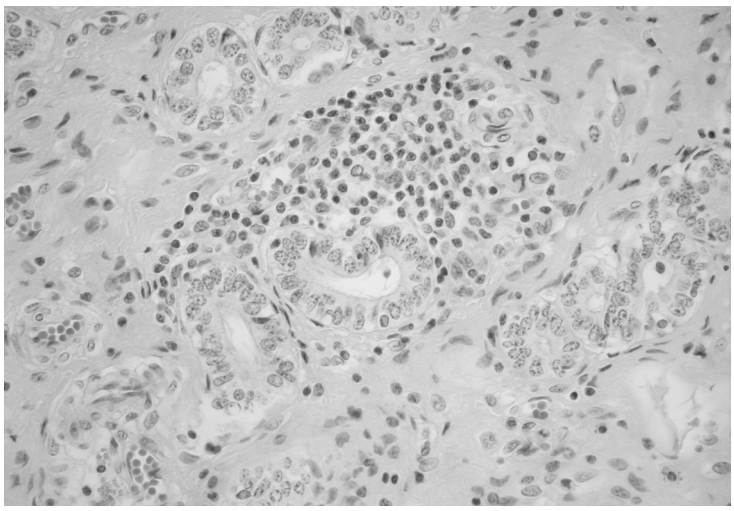

Fig. 1. Endometritis: periglandular lymphoplasmacytic infiltration (H.-E., × 400)

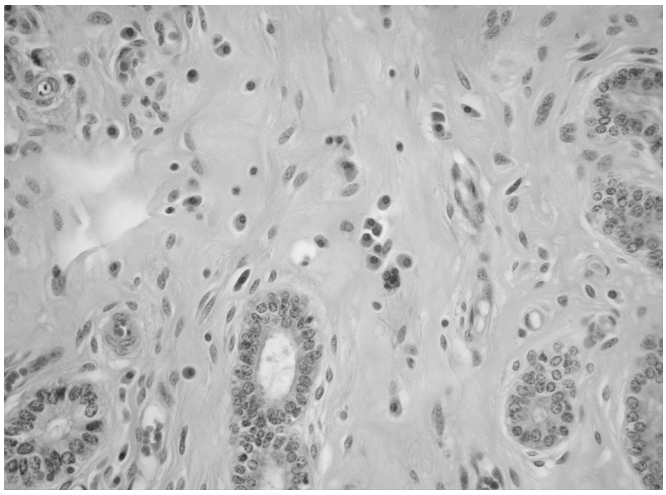

Fig. 2. Endometritis: plasmocytes in the stratum spongiosum (H.-E., × 400)

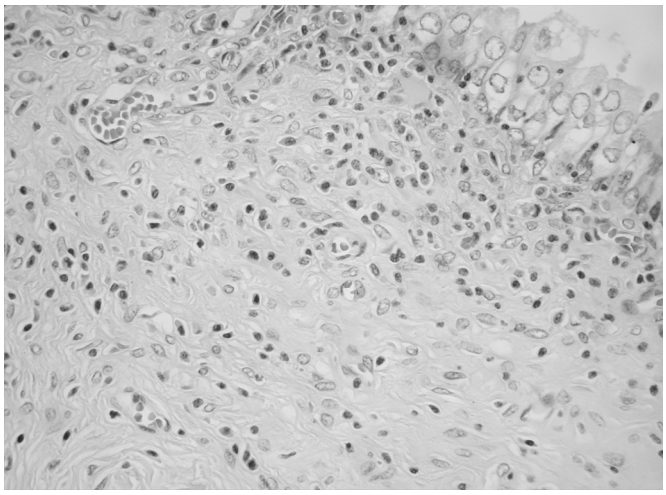

Fig. 3. Urocystitis: diffuse lymphoplasmacytic infiltration of the propria (H.-E., × 400)

Bacteriology

All urogenital tracts were examined within 5 hours of collection. Samples from both uterine horns, from the mid-cervix and urinary bladder were collected for bacteriological examinations with sterile cotton-tipped swabs. Swabs were streaked on blood-agar plates containing 5% sterile sheep or horse blood and a crystal violet-lactose-bromothymol blue agar plate media for aerobic culture at 37 °C for 24–48 h. For the isolation of *Eubacterium suis*, samples from the urinary bladder were inoculated on agar plates containing 5% sterile horse blood

without antibiotics and on colistin-nalidixic acid-metronidazole-supplemented Columbia blood-agar media (CCNAM) and incubated under anaerobic conditions at 37 °C for 7 days in a commercial anaerobic culture system (Oxoid Anaero Jars, Unipath GmbH). The same person evaluated all cultures; isolated bacteria were identified using standard methods (Barrow and Feltham, 1993). Cultures showing > 100 colonies/plate (pure or mixed culture) were considered positive; all other culture results were considered negative. Positive culture of one or both uterine horn samples or bladder sample indicated endometritis or urocystitis, respectively.

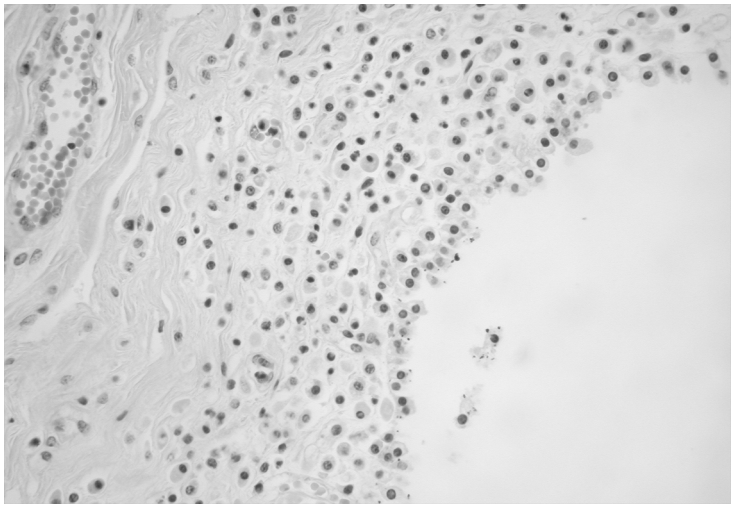

Fig. 4. Urocystitis: diffuse lymphoplasmacytic infiltration of the propria with epithelial desquamation (H.-E., × 400)

Statistical analysis

All data recorded and generated as above were checked twice for errors and were collected in Microsoft Excel spreadsheets.

We regarded histopathology results as the 'Gold Standard' to which macroscopic diagnostic and bacteriological culture results were compared. Sensitivity was defined as the proportion of true positives that are detected by the given method, while specificity was defined as the proportion of true negatives that are detected (Thrusfield, 1995). Sensitivity and specificity for culture result of uterine samples and/or macroscopic evaluation of endometrium, or culture result of bladder samples and/or macroscopic evaluation of bladder mucosa in relation to presence of endometritis and urocystitis, respectively, were calculated from 2 × 2 contingency tables (Martin, 1977; Martin et al., 1987; Thrusfield, 1995).

Data were stratified on parity (number of recorded farrowings) and stratum specific odds ratios (ORs) were calculated for the urocystitis (presumed 'exposure') and endometritis ('disease') relationship. A cut-off point of 5 was used for differentiation between 'high' and 'low' parity. We have also performed calculations with different parity cut-off points (i.e. 3, 4, 6 or more; data not shown). A crude overall odds ratio and the Mantel-Haenszel odds ratio, along with their confidence intervals were calculated to assess confounding possibly related to parity (Martin et al., 1987). Results were regarded significant at the $p < 0.05$ level.

Results

Prevalence of lesions and bacteriology

The prevalence of different lesions based on macroscopic, bacteriological or histopathological diagnoses are presented in Table 1. Briefly, the prevalence of endometritis diagnosed with macroscopic observation, bacteriology and histopathology was 3%, 25% and 16%, respectively. Corresponding values for urocystitis were 13%, 38% and 27%. Cystic ovaries, urocystitis and urinary calculi were the most frequent abnormalities encountered during macroscopic examination. In positive cases bacteriologic examination yielded pure or mixed cultures of enterobacteria, *Streptococcus* spp., *Staphylococcus* spp., *Proteus* spp., *Pseudomonas* spp., *Corynebacterium* spp. In three instances *Eubacterium suis* was detected in mixed culture from the bladder.

Statistical analysis

Sensitivity and specificity in case of macroscopic and/or bacteriological diagnosis of urocystitis and endometritis, compared to histopathological diagnosis as a 'Gold Standard' are presented in Table 2. Briefly, sensitivity of macroscopic observation and bacteriology alone in the case of endometritis were 18.1% and 31.8%, respectively. Sensitivity values were somewhat higher in the case of urocystitis: 47.9% and 63.0% for macroscopic diagnosis and bacteriology, respectively.

Data used in the analysis of the urocystitis – endometritis association, stratified for parity are presented in Table 3. The stratum-specific ORs could be combined into one summary OR because of the non-significance of the Breslow-Day test for similarity of stratum-specific ORs. There was no evidence of confounding as the crude summary OR and the Mantel-Haenszel OR (MHOR) did not differ. The MHOR was 3.44 (95% CI: 2.85, 4.13). Similar results were obtained when we defined different cut-off points, from parity 3, 4 and 6 and more and when performed a detailed stratification (from parity 0 to 6 and more, data not shown).

Table 1

Prevalence of macroscopic, bacteriological and histopathological findings in culled female breeding swine between 1995–2000 in Hungary

Variables	Total females	Range per herd	Prevalence	
			%	95% CI
Macroscopic findings				
Number examined	499	4–53		
Cervical developmental anomaly (aplasia)	2	0–2	0.4	0.0, 1.4
Cervicitis	12	0–3	2	1.2, 4.0
Concretions	54	0–11	11	8.3, 13.7
Cystic ovary (all forms)	50	0–10	10	7.4, 12.6
Endometritis, pyometra	16	0–5	3	1.8, 5.0
Hydrometra/mucometra	8	0–3	2	0.7, 3.1
Ovarian atrophy/inactivity	29	0–13	6	3.9, 8.1
Paraovarian cyst	16	0–5	3	1.8, 5.0
Pregnancy	15	0–8	3	1.6, 4.7
Urocystitis	66	0–9	13	10.0, 16
Uterine atrophy/inactivity	17	0–12	3	1.9, 5.2
Uterine developmental anomaly	6	0–5	1	0.4, 2.6
Miscellaneous oviduct abnormalities (hydrosalpinx/pyosalpinx, cyst, aplasia)	9	0–2	2	0.8, 3.3
Bacteriological findings				
Number examined	289	1–40		
Endometritis	73	0–14	25	20.0, 30.0
Urocystitis	111	0–15	38	32.4, 43.6
Histopathological findings				
Number examined	353	1–46		
Endometritis	55	0–9	16	12.2, 19.8
Urocystitis	96	0–15	27	22.4, 31.6

Discussion

Prevalence of detected lesions was similar in our study to what has been reported in the literature (McEntee, 1990; Dalin et al., 1997; Heinonen et al., 1998). Apart from ovarian cysts, urocystitis and concretions accounted for the majority of lesions. The prevalence of urocystitis was higher than the prevalence of endometritis in all examinations. However, large proportion of examined animals did not show any of the registered lesions. Bacteria isolated from the urinary bladder and endometrium represented members of the normal faecal flora, *Eubacterium suis* has been detected only in three instances.

Table 2

Sensitivity and specificity estimates for macroscopic and bacteriological diagnosis of endometritis and urocystitis as compared to histopathology in culled female breeding swine between 1995–2000 in Hungary

Disease	Number tested	Diagnostic method	Sensitivity		Specificity	
			%	95% CI	%	95% CI
Endometritis	353	Macroscopic	18.1	14.1, 22.1	96.6	94.7, 98.5
	289	Bacteriologic	31.8	26.4, 34.2	75.9	71.0, 80.8
	213	Macroscopic plus bacteriologic in parallel	18.7	13.5, 23.9	98.9	97.5, 100
Urocystitis	353	Macroscopic	47.9	42.7, 53.1	88.3	84.9, 97.1
	289	Bacteriologic	63.0	57.4, 68.6	71.0	57.4, 68.6
	182	Macroscopic plus bacteriologic in parallel	58.0	50.8, 65.2	96.2	50.8, 65.2

Table 3

Results of stratum specific analyses in the urocystitis – endometritis relationship in culled female breeding swine between 1995–2000 in Hungary

Parity	Urocystitis	Endometritis positive	Endometritis negative
≥ 5	positive	12	24
≥ 5	negative	7	56
< 5	positive	16	44
< 5	negative	20	174

Breslow-Day statistic for the similarity of stratum specific odds ratios (ORs) $\chi^2 = 0.13$, $p = 0.72$; Mantel-Haenszel odds ratio (MHOR) = 3.44; 95% confidence interval (CI) for MHOR = 2.85, 4.13

Both bacteriology and macroscopic observation alone were found to detect only a small proportion of animals with urocystitis or endometritis; the chance for false negative diagnosis was particularly high for macroscopic diagnosis of endometritis.

The low predictive value of a positive bacteriological culture in case of both organs probably reflects the effect of bacterial contamination. Bacterial contamination of the upper urinary and genital tracts during slaughterhouse sampling is an important problem (Meredith, 1986; Almond and Richards, 1992), which, as shown here, might influence negatively the validity of a diagnosis. Sensitivity and specificity figures could have been influenced by the method of macroscopic and bacteriological diagnosis of the mentioned conditions, as a certain level of subjectivity is unavoidable in such assessments. Nevertheless,

these results further emphasise the necessity of histopathology in the correct diagnosis of endometritis and urocystitis, and the beneficial effect of considering macroscopic and bacteriological test results together in order to estimate the true disease status of these organs. Histopathological diagnosis of urocystitis and endometritis was done somewhat subjectively, as there are no generally accepted diagnostic criteria for such lesions in swine. Unfortunately, virus-induced endometrial lesions in swine are practically indistinguishable from certain forms of bacterial endometritis (McEntee, 1990). However, we believe that histopathology still should be the 'Gold Standard' in such evaluations.

There was a strong statistical and epidemiological association between urocystitis and endometritis, which apparently was not confounded by parity. This supports the presumed association between urocystitis and endometritis. However, as it was a cross-sectional study, it was not possible to determine temporal relationships between the two conditions. Longitudinal studies would be required to clearly answer this question.

In summary, it appears from the results of our analyses that macroscopic or bacteriological examination of the urinary bladder or the uterus alone is likely to be not sufficient to arrive at a correct diagnosis of urocystitis or endometritis. Urocystitis and endometritis are strongly associated, which is not confounded by the parity of the animal. Animals with urocystitis had an approximately 3.5 times higher chance to simultaneously have endometritis than animals without this condition.

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