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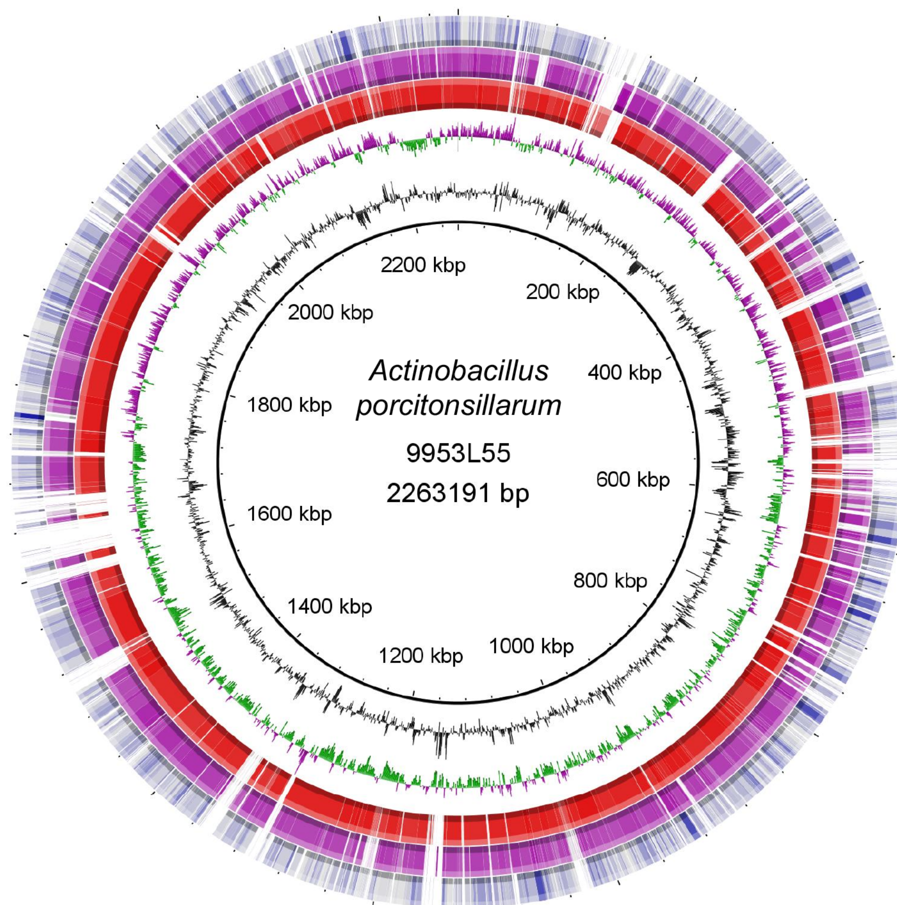
b UNIVERSITÄT BERN

ANNUAL REPORT 2018

Institute of Veterinary Bacteriology

Vetsuisse Faculty
Länggassstrasse 122
3012 Bern
Switzerland



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1 Preface

The Institute of Veterinary Bacteriology is delighted to distribute its Annual Report summarizing the activities and publications of 2018. It features the achievements of our staff, students and collaborators.

In 2018 we finalized research activities that were under the funding umbrellas of Swiss National Science Foundation and the Federal Food Safety and Veterinary Office devoted to research on *Listeria* as well as on abortion, respectively. In an effort to streamline research and to assure a critical mass we will focus our future research activities on antimicrobial resistance, molecular epidemiology, diseases of the hoof, *Mycoplasma* and synthetic genomics. We contributed towards 32 peer-reviewed publications. With respect to applied research we received a research grant from the private sector, which supports a postdoctoral scientist over two years.

Regarding our teaching commitments we taught students of the VETSUISSE and the SCIENCE faculty at the University of Bern and examined the latter orally. Besides the undergraduate education, we also contributed to postgraduate education, which is reflected by one master degree, two DVM degrees and one PhD degree. Additionally, we introduced the written exam in bacteriology, which was appreciated by the veterinary students. The three long-term colleagues Stefanie Gobeli, Paola Pilo and Sabrina Rodriguez-Campos left the institute. I would like to thank them for their contributions and wish them all the best for the future. In that context it has to be mentioned that Sabrina Rodriguez-Campos took on a professorship in Norway. In 2018 the veterinarian Lutz Schönecker started his residency.

Finally, we contributed to the provision of diagnostic services to the university, private practitioners and the Federal Food Safety and Veterinary Office (FSVO) as reference functions and monitoring of antibiotic resistance. I thank all members of the institute, its partners, and customers who made 2018 again a successful year for veterinary bacteriology in Bern.

Bern 17th September 2019 Jörg Jores

2 Research Units

2.1 Host-Pathogen Interactions

2.1.1 Pooling of interdigital swab samples for PCR diagnosis of virulent (*aprV2*) ovine footrot

Publication: Greber D, Locher I, Kuhnert P, Butty MA, Holdener K, Frey J, Schüpbach G, Steiner A. 2018. J Vet Diag Invest **30**:205-210. doi:/10.1177/104063871773350

Collaborators: Clinic for Ruminants, Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Switzerland; Veterinary Office of the Canton of Grisons, Chur, Switzerland

Abstract: Virulent ovine foot rot is a contagious foot disease. Given the development and validation of a real-time PCR to detect *Dichelobacter nodosus* isolates that contain the virulence-associated protease genes *aprV2* and *aprB2*, the diagnosis of foot rot has made considerable progress. We evaluated pooling methods to reduce the number of samples during a foot rot control program. Samples of individual feet were compared to a 4-feet sample of the same sheep. All further analyses based on 4-feet samples (pools-of-5 and pools-of-10 4-feet samples) were compared to samples of individual sheep, and a riskbased herd sampling was evaluated and compared to the whole flock. The sensitivity and specificity of the 4-feet samples for detection of *aprV2*-positive strains was 93.8% (CI: 87.6–97.5%) and 98.3% (CI: 96.5–99.3%), respectively. The sensitivity and specificity of the pools-of-10 was 86.7% (CI: 78.4–92.7%) and 100.0% (CI: 97.4–100%), respectively. Pools-of-5 were not significantly more sensitive than pools-of-10. The pooling of 4 individual foot samples into one 4-feet sample is an adequate method to reduce the number of samples of individual sheep. The sensitivity of pools-of-5 and pools-of-10 is too imprecise for a control program. Risk-based sampling allowed for a substantial reduction of samples to be tested, had a sensitivity of 95.8% (CI: 78.9–99.9%) and specificity of 100.0% (CI: 88.1–100.0%) when determining the foot rot flock status, and represents an adequate methodology to predict within-flock freedom from infection.

2.1.2 Potential transmission routes of *Dichelobacter nodosus*

Publication: Locher I,Giger L, Frosth S, Kuhnert P, Steiner A. 2018. Vet Microbiol **218**:20-24. doi:10.1016/j.vetmic.2018.03.024

Collaborators: Clinic for Ruminants, Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Switzerland; Department of Biomedical Sciences and Veterinary Public Health, Swedish University of Agricultural Sciences, Uppsala, Sweden

Abstract: Footrot caused by *Dichelobacter nodosus* is a highly contagious bacterial disease affecting the claw of sheep and the main cause of lameness in these animals. It is not only an economic burden but also a serious animal welfare issue. More information about the transmission of *D. nodosus* is needed for effective footrot control programs. We therefore determined the prevalence of D. nodosus in sheep presented at shows and markets where

commingling of animals occurs. Furthermore, possible transmission vectors during foot trimming were investigated and trimming knife decontamination protocols evaluated. Sheep at six markets and four shows were sampled and tested for the presence of D. nodosus by real-time PCR. Different vectors, such as trimming knives were tested by real-time PCR and for viable *D. nodosus* by culture. The prevalence of virulent *D. nodosus* in sheep presented at shows and markets ranged from 1.7% to 100%. Regions with an ongoing control program showed significantly lower prevalence. After trimming, positive real-time PCR and culture results were obtained from the knives, the hands of the claw trimmers as well as removed claw horn material whereas boots were only positive by real-time PCR. In conclusion, markets and shows pose a risk for transmission of *D. nodosus*. The risk of transmission is particularly high during claw trimming and recommended measures to limit this risk include wiping the knife with a disinfection towel, wearing and changing gloves after every sheep, as well as proper disposal of trimmed and infectious horn.

2.1.3 Detection of *Treponema pedis* associated with digital dermatitis in Mediterranean buffalo (*Bubalus bubalis*)

Publication: Guccione J, Della Valle G, Carcasole C, Kuhnert P, Alsaaod M. 2018. Vet Rec Case Rep **6**:e000674. doi:10.1136/vetreccr-2018-000674

Collaborators: Department of Veterinary Medicine and Animal Productions, University of Napoli Federico II, Napoli, Italy

Abstract: Clinical outcomes compatible with digital dermatitis (DD) were observed in a second lactation, milking Mediterranean buffalo (MB). The animal was sharing the free stall with other 99 milking MBs separated by a fence from a pen harbouring 40 milking crossbreed dairy cows. The macroscopic lesion observed on the right rear limb was categorised as M4.1 stage and associated with a severe lameness (locomotion score 5). In the same farm, DD was also observed in 14/40 cows. Nested PCR analysis of genomic DNA isolated from the centre lesion's biopsy showed the presence of *Treponema pedis*. Sequence analysis of 494 bp of the PCR fragment revealed 100 per cent sequence identity to the *T. pedis* type strain, confirming the PCR result's specificity and for the first time the presence of the bacterium in MB. In order to establish the spread of the DD, a farm inspection was performed to identify risk factors and preventive strategies.

2.1.4 *Mycoplasma hyopneumoniae* infections in pigs: knowledge gaps for improved disease control

Publication: Maes D, Sibila M, Kuhnert P, Segalés J, Haesebrouck F, Pieters M. 2018. Transbound Emerg Dis **65** Suppl 1:110-124. doi:10.1111/tbed.12677.

Collaborators: Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium; Universitat Autonoma de Barcelona, Bellaterra, Spain; Department of Veterinary Population Medicine, College of Veterinary Medicine, University of Minnesota, USA

Abstract: Mycoplasma hyopneumoniae (*M. hyopneumoniae*) is the primary pathogen of enzootic pneumonia, a chronic respiratory disease in pigs. Infections occur worldwide and cause major economic losses to the pig industry. The present paper reviews the current knowledge on *M. hyopneumoniae* infections, with emphasis on identification and analysis of knowledge gaps for optimizing control of the disease. Close contact between infected and susceptible pigs is the main route of *M. hyopneumoniae* transmission. Management and housing conditions predisposing for infection or disease are known, but further research is needed to better understand *M. hyopneumoniae* transmission patterns in modern pig production systems, and to assess the importance of the breeding population for downstream disease control. The organism is primarily found on the mucosal surface of the trachea, bronchi and bronchioles. Different adhesins and lipoproteins are involved in the adherence process. However, a clear picture of the virulence and pathogenicity of *M. hyopneumoniae* is still missing. The role of glycerol metabolism, myoinositol metabolism and the *Mycoplasma* Ig binding protein—*Mycoplasma* Ig protease system should be further investigated for their contribution to virulence. The destruction of the mucociliary apparatus, together with modulating the immune response, enhances the susceptibility of infected pigs to secondary pathogens. Clinical signs and severity of lesions depend on different factors, such as management, environmental conditions and likely also *M. hyopneumoniae* strain. The potential impact of strain variability on disease severity is not well defined. Diagnostics could be improved by developing tests that may detect virulent strains, by improving sampling in live animals and by designing ELISAs allowing discrimination between infected and vaccinated pigs. The currently available vaccines are often cost-efficient, but the ongoing research on developing new vaccines that confer protective immunity and reduce transmission should be continued, as well as optimization of protocols to eliminate *M. hyopneumoniae* from pig herds.

2.1.5 Whole-genome-based revisit of *Photorhabdus* phylogeny: proposal for the elevation of most *Photorhabdus* subspecies to the species level and description of one novel species *Photorhabdus bodei* sp. nov., and one novel subspecies *Photorhabdus laumondii* subsp. *clarkei* subsp. nov.

Publication: Machado RAR, Wüthrich D, Kuhnert P, Arce CCM, Thönen L, Ruiz C, Zhang NX, Robert CAM, Karimi J, Kamali S, Ma J, Bruggmann R, Erb M. 2018. Int J Syst Evol Microbiol **68**:2664-2681. doi:10.1099/ijsem.0.002820

Collaborators: Institute of Plant Sciences, University of Bern, Bern, Switzerland

Abstract: Bacterial symbionts are crucial for the infectivity and success of entomopathogenic nematodes as biological control agents. The current understanding of the symbiotic

relationships is limited by taxonomic uncertainties. Here, we used whole-genome sequencing and traditional techniques to reconstruct the phylogenetic relationships between all described *Photorhabdus* species and subspecies as well as 11 newly isolated symbiotic bacteria of *Heterorhabditis* nematodes, including the unreported bacterial partner of *H. beicherriana. In silico* DNA–DNA hybridization, orthologous average nucleotide identity and nucleotide sequence identity of concatenated housekeeping genes scores were calculated and set into relation with current cut-off values for species delimitation in bacteria. Sequence data were complemented with biochemical and chemotaxonomic markers, and ribosomal protein fingerprinting profiles. This polyphasic approach resolves the ambiguous taxonomy of *Photorhabdus* and lead to the proposal for the elevation of most of them into a higher taxon and the creation of several new taxa: 15 new species, one of which is newly described: *Photorhabdus bodei* sp. nov. (type strain LJ24-63T=DSM 105690T=CCOS 1159T) and the other 14 arise through the proposal of elevating already described subspecies to species, and are proposed to be renamed as follows: *Photorhabdus asymbiotica* subsp. *australis* as *Photorhabdus australis* sp. nov., *Photorhabdus luminescens* subsp. *akhurstii* as *Photorhabdus akhurstii* sp. nov., *Photorhabdus luminescens* subsp. *caribbeanensis* as *Photorhabdus caribbeanensis* sp. nov., *Photorhabdus luminescens* subsp. *hainanensis* as *Photorhabdus hainanensis* sp. nov., *Photorhabdus luminescens* subsp. *kayaii* as *Photorhabdus kayaii* sp. nov., *Photorhabdus luminescens* subsp. *kleinii* as *Photorhabdus kleinii* sp. nov., *Photorhabdus luminescens* subsp. *namnaonensis* as *Photorhabdus namnaonensis* sp. nov., *Photorhabdus luminescens* subsp. *noenieputensis* as *Photorhabdus noenieputensis* sp. nov., *Photorhabdus luminescens* subsp. *laumondii* as *Photorhabdus laumondii* sp. nov., *Photorhabdus temperate* subsp. *cinerea* as *Photorhabdus cinerea* sp. nov., *Photorhabdus temperata* subsp. *khanii* as *Photorhabdus khanii* sp. nov., *Photorhabdus temperata* subsp. *stackebrandtii* as *Photorhabdus stackebrandtii* sp. nov., *Photorhabdus temperata* subsp. *tasmaniensis* as *Photorhabdus tasmaniensis* sp. nov., and *Photorhabdus temperata* subsp. *thracensis as Photorhabdus thracensis* sp. nov. In addition, we propose the creation of two new subspecies, one of which arises through the reduction of rank: *Photorhabdus laumondii* subsp. *laumondii* comb. nov. (basonym: *P. luminescens* subsp. *laumondii*) and the second one is newly described: *Photorhabdus laumondii* subsp. *clarkei* subsp. nov. (type strain BOJ-47T=DSM 105531T=CCOS 1160T). Finally, we propose to emend the description of three species, which results from the proposal of elevating three subspecies to the species status: *Photorhabdus asymbiotica*, *Photorhabdus temperata* and *Photorhabdus luminescens*, formerly classified as *Photorhabdus asymbiotica* subsp. *asymbiotica*, *Photorhabdus temperata* subsp. *temperata* and *Photorhabdus luminescens* subsp. *luminescens*, respectively.

2.1.6 Limited added value of fungal ITS amplicon sequencing in the study of bovine

abortion.

Publication: Vidal S, Brandt BW, Dettwiler M, Abril C, Bressan J, Greub G, Frey CF, Perreten V, Rodriguez-Campos S. 2018. Heliyon. **4**(11):e00915. *doi*: 10.1016/j.heliyon.2018.e00915.

Collaborators: Department of Preventive Dentistry, Academic Centre for Dentistry Amsterdam, University of Amsterdam and VU University Amsterdam, Amsterdam, the Netherlands; Institute of Animal Pathology, Vetsuisse Faculty, University of Bern, Bern, Switzerland; Institute of Virology and Immunology, University of Bern, Bern, Switzerland; Department of Neurology, Bern University Hospital and University of Bern, Bern, Switzerland; Institute of Microbiology, University Hospital Center and University of Lausanne, Lausanne, Switzerland; Institute of Parasitology, Vetsuisse Faculty, University of Bern, Bern, Switzerland.

Abstract: Bovine mycotic abortion is sporadic and caused by different ubiquitous and opportunistic fungi. Recently, a broad spectrum of bacterial opportunists involved in bovine abortion was revealed by 16S rRNA gene amplicon sequencing. We hypothesized that fungal organisms potentially involved in bovine abortion also might remain undetected by conventional culture. In this retrospective study, we therefore applied fungal internal transcribed spacer 2 (ITS2) region amplicon sequencing to 74 cases of bovine abortion submitted to our diagnostic service. The investigation was complemented by fungal culture and, retrospectively, by data from bacteriological, virological and parasitological analyses and histopathological examination of placentas. Fungal DNA was found in both the placentas and abomasal contents, with 92 fungal genera identified. In 18 cases, >75% of the reads belonged to one specific fungal genus: *Candida* (n = 7), *Malassezia* (n = 4), *Cryptococcus* (n = 3), unidentified *Capnodiales* (n = 3), *Actinomucor* (n = 1), *Cystofilobasidium* (n = 1), *Penicillium* (n = 1), *Verticillum* (n = 1) and *Zymoseptoria* (n = 1) with one case harboring two different genera. By culture, in contrast, fungal agents were detected in only 6 cases. Inflammatory and/or necrotizing lesions were found in 27/40 histologically assessed placentas. However, no lesion-associated fungal structures were detected in HE- and PAS-stained specimens. Complementary data revealed the presence of one or more non-fungal possible abortifacient: *Chlamydiales*, *Coxiella burnetii*, *Leptospira* spp., *Campylobacter fetus* subsp. *fetus*, *Streptococcus uberis*, *Escherichia coli*, *Streptococcus pluranimalium*, *Bacillus licheniformis*, *Campylobacter fetus* subsp. *fetus*, *Serratia marcescens*, *Trueperella pyogenes*, Schmallenbergvirus, *Neospora caninum*. The mycobiota revealed by sequencing did not differ between cases with or without a possible infectious etiology. Our study suggests that amplicon sequencing of the ITS2 region from DNA isolated from bovine abortion does not provide additional information or new insight into mycotic abortion and without complementary analyses may easily lead to a false interpretation of the role of fungal organisms in bovine abortion.

2.1.7 Identification of targets of monoclonal antibodies that inhibit adhesion and

growth in *Mycoplasma mycoides* subspecies *mycoides*

Publication: Aye R, Weldearegay YB, Lutta HO, Chuma F, Pich A, Jores J, Meens J, Naessens J. 2018. Vet Immunol Immunopathol **204**:11-18, *doi:* 10.1016/j.vetimm.2018.09.002.

Collaborators: International Livestock Research Institute, Nairobi, Kenya; Kenya Agricultural and Livestock Research Organization, Nairobi, Kenya; University of Veterinary Medicine Hannover, Foundation, Hannover, Germany; Hannover Medical School, Hannover, Germany

Abstract: Mycoplasma mycoides subspecies *mycoides* (*Mmm*) adhesion is tissue and host specific. Inhibition of adhesion will prevent *Mmm* from binding to lung cells and hence prevent colonization and disease. The aim of this study was to develop a panel of *Mmm* monoclonal antibodies against *Mmm* and use these antibodies to investigate their inhibitory effect on the adherence of *Mmm* to bovine lung epithelial cells (BoLEC), and to further identify an antigen to any of the inhibitory antibodies. Thirteen anti-*Mycoplasma mycoides* subsp. *mycoides* (AMMY) monoclonal antibodies (mAbs) inhibited adhesion by at least 30% and ten of the mAbs bound to multiple bands on Western blots suggesting that the antibodies bound to proteins of variable sizes. AMMY 10, a previously characterized *Mmm*- capsular polysaccharide (CPS) specific antibody, inhibited growth of Mmm in vitro and also caused agglutination of Mmm total cell lysate. AMMY 5, a 2-oxo acid dehydrogenase acyltransferase (Catalytic domain) (MSC_0267) specific antibody, was identified and polyclonal rabbit serum against recombinant MSC_0267 blocked adhesion of Mmm to BoLEC by 41%. Antigens recognized by these antibodies could be vaccine candidate(s) and should be subsequently tested for their ability to induce a protective immune response in vivo.

2.2 Molecular and Bacterial Epidemiology and Infectious Diseases

2.2.1 Predominance of a macrolide-lincosamide-resistant *Brachyspira hyodysenteriae* of sequence type 196 in Swiss pig herds

Publication: García-Martín AB, Perreten V, Rossano A, Schmitt S, Nathues H, Zeeh F. 2018. Vet Microbiol. **226**:97-102. *doi*: 10.1016/j.vetmic.2018.10.007.

Collaborators: Clinic for Swine, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland; Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland.

Abstract: Worldwide emergence of antimicrobial-resistant *Brachyspira* (*B.*) *hyodysenteriae* led us question whether specific clones are present in Switzerland. Fifty-one *B. hyodysenteriae* isolates originating from 27 different Swiss pig herds sampled between 2010 and 2017 were characterised. Multilocus sequence typing revealed the presence of four different sequence types (STs) ST6, ST66, ST196 and ST197 with ST196 being predominant. Antimicrobial susceptibility to six different antimicrobial agents was determined by measurement of the minimal inhibitory concentration by broth dilution. Isolates were examined for the presence of

point mutations and genes known to be associated with antimicrobial resistance in *B. hyodysenteriae* by PCR and sequence analysis. Forty-one isolates belonging to ST6 (n = 1), ST66 (n = 4) and ST196 (n = 36) exhibited decreased susceptibility to macrolides and lincomycin associated with an A2058 T/G mutation in the 23S rRNA gene. One isolate of ST66 and five isolates of ST196 exhibited decreased susceptibility to doxycycline associated with a G1058C mutation in the 16S rRNA gene. The Swiss B. hyodysenteriae population is characterised by a low genetic diversity, with macrolide-lincosamide-resistant isolates of ST196 being predominant.

2.2.2 Antimicrobial susceptibility patterns of blood culture isolates from foals in Switzerland

Publication: Fouché N, Gerber V, Thomann A, Perreten V. 2018. Schweiz Arch Tierheilkd. **160**(11):665-671. *doi:* 10.17236/sat00184.

Collaborators: Swiss Institute of Equine Medicine (ISME), Vetsuisse Faculty, University of Bern, and Agroscope, Switzerland.

Abstract: We report blood culture results of 43 foals admitted to an equine hospital for medical or surgical disorders and determine minimal inhibitory concentrations (MIC) of different antibiotics. Eleven foals had a positive blood culture result despite prior administration of antibiotics in 10 of these animals. MIC values above EUCAST and/or CLSI breakpoints were identified in coagulase-negative staphylococci, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Enterococcus faecium*. Gram-negative isolates were less frequently identified and did not appear to exhibit increased MIC values. This study shows that bloodstream infections in foals in Switzerland are caused by diverse bacteria including Gram-positive bacteria which exhibit resistance to several classes of antibiotics.

2.2.3 Comparative genomics of the first and complete genome of "*Actinobacillus porcitonsillarum*" supports the novel species hypothesis

Publication: Donà V, Perreten V. 2018. Int J Genomics **2018**:5261719. *doi*: 10.1155/2018/5261719.

Collaborators: N/A

Abstract: "*Actinobacillus porcitonsillarum*" is considered a nonpathogenic member of the *Pasteurellaceae* family, which phenotypically resembles the pathogen *Actinobacillus pleuropneumoniae*. Previous studies suggested that "*A. porcitonsillarum*" may represent a new species closely related to *Actinobacillus minor*, yet no full genome has been sequenced so far. We implemented the Oxford Nanopore and Illumina sequencing technologies to obtain the highly accurate and complete genome sequence of the "*A. porcitonsillarum*" strain 9953L55. After validating our *de novo* assembly strategy by comparing the *A. pleuropneumoniae* $S4074^T$ genome sequence obtained by Oxford Nanopore Technology combined with Illumina reads

with a PacBio-sequenced S4074^T genome from the NCBI database, we performed comparative analyses of the 9953L55 genome with the *A. minor* type strain NM305^T, *A. minor* strain 202, and *A. pleuropneumoniae* S4074^T. The 2,263,191 bp circular genome of 9953L55 consisted of 2168 and 2033 predicted genes and proteins, respectively. The lipopolysaccharide cluster resembled the genetic organization of *A. pleuropneumoniae* serotypes 1, 9, and 11, possibly explaining the positive reactions observed previously in serotyping tests. In contrast to NM305^T, we confirmed the presence of a complete *apxIICABD* operon in 9953L55 and 202 accounting for their hemolytic phenotype and Christie-Atkins-Munch-Petersen (CAMP) reaction positivity. Orthologous gene cluster analysis provided insight into the differential ability of strains of the *A. minor*/"*porcitonsillarum*" complex and *A. pleuropneumoniae* to ferment lactose, raffinose, trehalose, and mannitol. The four strains showed distinct and shared transposable elements, CRISPR/Cas systems, and integrated prophages. Genome comparisons based on average nucleotide identity and *in silico* DNA-DNA hybridization confirmed the close relationship among strains belonging to the *A. minor*/"*porcitonsillarum*" complex compared to other *Actinobacillus* spp., but also suggested that 9953L55 and 202 belong to the same novel species closely related to *A. minor*, namely, "*A. porcitonsillarum*." Recognition of the taxon as a separate species would improve diagnostics and control strategies of pig pleuropneumonia.

2.2.4 The integrase of the *Macrococcus caseolyticus* resistance island *mecD* (McRI$_{mecD}$) inserts DNA site-specifically into *Staphylococcus* and *Bacillus* chromosomes

Publication: Schwendener S, Perreten V. 2018. Mol Microbiol. **110**(3):455-468. *doi*: 10.1111/mmi.14112.

Collaborators: N/A

Abstract: The methicillin resistance gene *mecD* has been recently identified on chromosomal islands in *Macrococcus caseolyticus* (McRI$_{mecD}$). The 5' end of McRI$_{mecD}$ carries an integrase (int) of the tyrosine recombinase family and two genes (*intR* and *xis*) encoding putative DNA-binding proteins. The islands are integrated site-specifically at the 3' end of the rpsI gene, a highly conserved locus in Gram-positive bacteria. Moreover, the *rpsI* gene of some *Staphylococcus* and *Bacillus* strains was found to be followed by a related integrase, raising the question of whether McRI$_{mecD}$ could be transferred to these species. We used circular model elements carrying 5' end fragments of McRI$_{mecD}$-1 to demonstrate that the int enzyme and the attachment (*att*) site were sufficient to mediate site-specific DNA integration into the rpsI locus of *Staphylococcus aureus*, *Staphylococcus pseudintermedius* and *Bacillus thuringiensis* in vivo. Including *xis* in the model element stimulated both integrative and excisive recombination reactions and influenced the Int enzyme in *att* site selection. The intR gene functions as a negative regulator of *int* and *xis*. The int-xis genes of McRI$_{mecD}$-1 encode a site-specific recombination function that enables the acquisition of McRI$_{mecD}$ in new hosts and the potential dissemination of broad-spectrum β-lactam resistance across genus barriers.

2.2.5 Extensively drug-resistant community-acquired *Acinetobacter baumannii* sequence type 2 in a dog with urinary tract infection in Thailand

Publication: Chanchaithong P, Prapasarakul N, Sirisopit Mehl N, Suanpairintr N, Teankum K, Collaud A, Endimiani A, Perreten V. 2018. J Glob Antimicrob Resist. **13**:33-34. *doi*: 10.1016/j.jgar.2018.02.007.

Collaborators: Department of Veterinary Microbiology, Department of Veterinary Surgery, Department of Veterinary Pharmacology and Department of Veterinary Pathology, Faculty of Veterinary Science, Chulalongkorn University, Bangkok 10330, Thailand; Institute for Infectious Diseases, Faculty of Medicine, University of Bern, Bern, Switzerland

Abstract: This study describes the first detection of an extensively drug-resistant *A. baumannii* isolated from a dog with urinary tract infection (UTI) in Thailand. The isolate was non-susceptible to all tested antibiotics including piperacillin, ticarcillin-clavulanic acid ceftazidime, cefepime, cefotaxime, imipenem, meropenem, gentamicin, amikacin, tetracycline, doxycycline, ciprofloxacinand trimethoprim/sulfamethoxazole, except for colistin. *A. baumannii* belongs to ST2 and contains the carbapenemase gene $bla_{\text{OXA-23}}$ on Tn*2006* and represents one of the most common lineages in human hospitals, suggesting a possible human-to-animal transmission.

2.2.6 Transposon-associated lincosamide resistance *lnu*(C) gene identified in *Brachyspira hyodysenteriae* ST83

Publication: De Luca S, Nicholson P, Magistrali CF, García-Martín AB, Rychener L, Zeeh F, Frey J, Perreten V. 2018. Vet Microbiol. **214**:51-55. *doi*: 10.1016/j.vetmic.2017.12.003.

Collaborators: Department of Veterinary Medicine, University of Perugia, Perugia, Italy; Istituto Zooprofilattico dell'Umbria e delle Marche, Perugia, Italy. Clinic for Swine, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland.

Abstract: Treatment of Swine Dysentery (SD) caused by *Brachyspira hyodysenteriae* (*B. hyodysenteriae)* is carried out using antimicrobials such as macrolides, lincosamides and pleuromutilins leading to the selection of resistant strains. Whole genome sequencing of a multidrug-resistant *B. hyodysenteriae* strain called BH718 belonging to sequence type (ST) 83 revealed the presence of the lincosamide resistance gene *lnu*(C) on the small 1724-bp transposon MTnSag1. The strain also contains an A to T substitution at position 2058 (A2058T) in the 23S rRNA gene which is known to be associated with macrolide and lincosamide resistance in *B. hyodysenteriae*. Testing of additional strains showed that those containing *lnu*(C) exhibited a higher minimal inhibitory concentration (MIC) of lincomycin (MIC $\geq$ 64 mg/L) compared to strains lacking *lnu*(C), even if they also harbor the A2058T mutation. Resistance to pleuromutilins could not be explained by the presence of already

reported mutations in the 23S rRNA gene and in the ribosomal protein L3. This study shows that *B. hyodysenteriae* has the ability to acquire mobile genetic elements conferring resistance to antibiotics.

2.2.7 Complete genome sequence of the type strain of *Macrococcus canis*

Publication: Gobeli Brawand S, Rychener L, Schwendener S, Pantůček R, Perreten V. 2018. Genome Announc. **6**(3). pii: e01507-17. *doi*: 10.1128/genomeA.01507-17.

Collaborators: Department of Experimental Biology, Faculty of Science, Masaryk University, Brno, Czech Republic.

Abstract: The first complete genome sequence of the recently described *Macrococcus canis* species has been determined for the strain KM45013^T (=DSM 101690^T = CCOS 969^T = CCUG 68920^T = CCM 8748^T). The strain was isolated from a dog with rhinitis and contains a putative γ-hemolysin and a *mecB*-carrying staphylococcal cassette chromosome *mec* element (SCC*mec*$_{KM45013}$).

2.2.8 Studies in collaboration with other institutions

2.2.8.1 Improving the quality and workflow of bacterial genome sequencing and analysis: paving the way for a Switzerland-wide molecular epidemiological surveillance platform.

Publication: Egli A, Blanc DS, Greub G, Keller PM, Lazarevic V, Lebrand A, Leib S, Neher RA, Perreten V, Ramette A, Schrenzel J, Stephan R, Wagner K, Wuethrich D, Xenarios I. Swiss Med Wkly. 2018 Dec 15;148:w14693. *doi*: 10.4414/smw.2018.14693.

Collaborators: Division of Clinical Microbiology, University Hospital Basel, Switzerland; Applied Microbiology Research, Department of Biomedicine, University of Basel, Switzerland; Hospital Preventive Medicine Service, Lausanne University Hospital, Switzerland; Institute for Microbiology, Lausanne University Hospital, Switzerland; Institute of Microbiology, University of Zurich, Switzerland; Bacteriology Laboratory, Division of Laboratory Medicine, Department of Genetics Laboratory Medicine and Pathology, Geneva University Hospitals, Switzerland; SIB Swiss Institute of Bioinformatics, Lausanne, Switzerland; Biozentrum, University of Basel, Switzerland; Institute for Infectious Diseases, University of Bern, Switzerland; Swiss Centre for Antibiotic Resistance (anresis.ch), Institut für Infektionskrankheiten, University of Bern, Switzerland; Genomic Research Laboratory, Division of Infectious Diseases, Geneva University Hospitals, Switzerland; Institute for Food Safety, Vetsuisse Faculty, University of Zurich, Switzerland.

2.2.8.2 Evaluation of EDTA- and DPA-based microdilution phenotypic tests for the

detection of MCR-mediated colistin resistance in *Enterobacteriaceae*

Publication: Büdel T, Clément M, Bernasconi OJ, Principe L, Perreten V, Luzzaro F, Endimiani A. 2019. Evaluation of EDTA- and DPA-based microdilution phenotypic tests for the detection of MCR-mediated colistin resistance in *Enterobacteriaceae*. Microb Drug Resist. **25**(4):494-500. *doi*: 10.1089/mdr.2018.0275.

Collaborators: Institute for Infectious Diseases, University of Bern, Bern, Switzerland; Graduate School of Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland; Clinical Microbiology and Virology Unit, A. Manzoni Hospital, Lecco, Italy.

2.2.8.3 Characterization of staphylococcal cassette chromosome *mec* elements from methicillin-resistant *Staphylococcus pseudintermedius* infections in Australian animals

Publication: Worthing KA, Schwendener S, Perreten V, Saputra S, Coombs GW, Pang S, Davies MR, Abraham S, Trott DJ, Norris JM. 2018. mSphere. **3**(6). pii: e00491-18. *doi*: 10.1128/mSphere.00491-18.

Collaborators: Sydney School of Veterinary Science, University of Sydney, NSW, Australia; Department of Microbiology and Immunology, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, VIC, Australia; Australian Centre for Antimicrobial Resistance Ecology, School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, SA, Australia; Research Center for Biology, Indonesian Institute of Sciences, Bogor, Indonesia; Australia Antimicrobial Resistance and Infectious Diseases Laboratory, School of Veterinary Life Sciences, Murdoch University, Murdoch, WA, Australia; PathWest Laboratory Medicine-WA, Fiona Stanley Hospital, Murdoch, WA, Australia.

2.2.8.4 The EDTA-based disk-combination tests are unreliable for the detection of MCR-mediated colistin-resistance in *Enterobacteriaceae*

Publication: Clément M, Büdel T, Bernasconi OJ, Principe L, Perreten V, Luzzaro F, Endimiani A. 2018. J Microbiol Methods. **153**:31-34. *doi*: 10.1016/j.mimet.2018.08.008.

Collaborators: Institute for Infectious Diseases, University of Bern, Bern, Switzerland; Graduate School of Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland; Clinical Microbiology and Virology Unit, A. Manzoni Hospital, Lecco, Italy.

2.2.8.5 Multiresistant *Brachyspira hyodysenteriae* shedding by pigs during the fattening period

Publication: Massacci FR, De Luca S, Cucco L, Tentellini M, Perreten V, Pezzotti G, Magistrali CF. 2018. Vet Rec. **183**(8):264. *doi*: 10.1136/vr.104886.

Collaborators: Research and Development Unit, Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, Perugia, Umbria, Italy.

2.2.8.6 Lack of intramammary niche recolonization during a sanitation program for the contagious mastitis pathogen *Staphylococcus aureus* genotype B.

Publication: Sartori C, Perreten V, Ivanovic I, Härdi-Landerer MC, Graber HU. 2018. J Dairy Sci. **101**(9):8296-8300. *doi*: 10.3168/jds.2017-14313.

Collaborators: Food Microbial Systems, Group Microbiological Safety of Foods of Animal Origin, Agroscope, Berne, Switzerland; Institute of Agricultural Sciences (IAS), Animal Physiology Group, ETH Zurich, Zurich, Switzerland.

2.2.8.7 Isolation of *Brachyspira hyodysenteriae* from a crow (*Corvus corone*) in close proximity to commercial pigs.

Publication: Zeeh F, Klausmann S, Masserey Y, Nathues H, Perreten V, Rohde J. 2018. Vet J. Jun;236:111-112. doi: 10.1016/j.tvjl.2018.05.002.

Collaborators: Clinic for Swine, Vetsuisse Faculty, University of Bern, Bern, Switzerland; SUISAG, Pig Health Service, 6204 Sempach, Switzerland; Institute for Microbiology, University of Veterinary Medicine, Foundation, Hannover, Germany.

2.2.8.8 Intestinal colonisation with extended-spectrum cephalosporin-resistant *Enterobacteriaceae* in different populations in Switzerland: prevalence, risk factors and molecular features.

Publication: Pires J, Kuenzli E, Hauser C, Tinguely R, Kasraian S, Atkinson A, Rauch A, Furrer H, Perreten V, Marschall J, Hatz C, Endimiani A. 2018. J Glob Antimicrob Resist. **12**:17-19. *doi*: 10.1016/j.jgar.2017.11.007

Collaborators: Institute for Infectious Diseases (IFIK), University of Bern, Bern, Switzerland; Graduate School of Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland; Swiss Tropical and Public Health Institute, Basel, Switzerland; Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland; Department of Infectious Diseases, Bern University Hospital and University of Bern, Bern, Switzerland.

2.2.8.9 Deciphering the complete deletion of the *mgrB* locus in an unusual colistin-resistant *Klebsiella pneumoniae* isolate colonising the gut of a traveller returning from India.

Publication: Bernasconi OJ, Donà V, Pires J, Kuenzli E, Hatz C, Luzzaro F, Perreten V, Endimiani A. 2018. Int J Antimicrob Agents. **51**(3):529-531. *doi*: 10.1016/j.ijantimicag.2017.09.014.

Collaborators: Institute for Infectious Diseases, University of Bern, Bern, Switzerland; Graduate School of Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland; Swiss Tropical and Public Health Institute, Basel, Switzerland; Division of Communicable

Diseases, Institute for Social and Preventive Medicine, University of Zurich, Zurich, Switzerland; Laboratory of Microbiology, A. Manzoni Hospital, Lecco, Italy.

2.2.8.10 ***Brachyspira hyodysenteriae* detection in the large intestine of slaughtered pigs.**

Publication: Zeeh F, De Luca S, Nicholson P, Grützner N, Nathues C, Perreten V, Nathues H. 2018. J Vet Diagn Invest. **30**(1):56-63. *doi*: 10.1177/1040638717722816.

Collaborators: Clinic for Swine, Vetsuisse Faculty, University of Bern, Switzerland; Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Switzerland; Faculty of Veterinary Medicine, University of Perugia, Perugia, Italy

3 ZOBA – Centre for Zoonoses, Bacterial Epizootics and Antimicrobial Resistance

In ZOBA encompasses the two subdivisions (i) 'Diagnostic Services and Epizootic Surveillance'and (ii) 'Reference Laboratories and Antimicrobial Resistance Monitoring'. The two subdivisons analysed a total of 20104 samples. Details are shown in Table 1.

Table 1: Number of investigated samples listed per unit of the two subdivisions

Subdivision	Unit	Number of samples
Diagnostic Services and Epizootic Surveillance	Clinical material and mycology	2961
	Necropsy material, abortion and feaces	2774
	Molecular diagnostics (PCR incl. qPCR)	1462
	Bovine mastitis	3253
	Serology	2553
	Species identification	992
	Antibiograms for diagnostics	1724
Reference Laboratories and Resistance Monitoring	Antimicrobial resistance monitoring (detection)	2728
	Antimicrobial resistance monitoring (MIC*)	1043
	Reference laboratories	614

* Minimal inhibitory concentration

3.1 Diagnostic Services and Epizootic Surveillance (Notifiable Animal Diseases)

Methods:

Micr	Microscopic examination
IF	Immunofluorescence
Cult	Culture
ELISA	Antibody detection by Enzyme-Linked Immunosorbent Assay
RBT	Antibody detection by Rose Bengal test
CFT	Antibody detection by complement fixation test
MAT	Antibody detection by the microscopic agglutination test
LF	Antibody detection by lateral flow test

PCR	Polymerase chain reaction
SEQ	Sequencing
ST	Serotyping (* in human reference laboratory)

3.1.1 Highly infectious epizootics

Table 2: Number of samples investigated related to highly infectious epizootics

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Contagious Bovine Pleuropneumonia	*Mycoplasma mycoides* subsp. *mycoides*	Cult	**Cattle**	0	0	0	0
		PCR		0	0	0	0
		ELISA		0	0	0	0

3.1.2 Epizootics to be eradicated

Table 3: Number of samples investigated related to epizootics to be eradicated

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Anthrax	*Bacillus anthracis*	Micr	**Cattle**	19	19	0	0
		Cult		22	22	0	0
	Bacillus anthracis	Micr	**Swine**	2	2	0	0
		Cult		2	2	0	0
	Bacillus anthracis	Micr	**Deer**	1	1	0	0
		Cult		1	1	0	0
Brucellosis	*Brucella abortus*	Micr	**Cattle**	102	100	2	0
		RBT		5	5	0	0
		ELISA		695	695	0	0
		CFT		0	0	0	0
	Brucella melitensis	Micr	**Sheep/goat**	54	46	8	0
		ELISA		30	30	0	0
		CFT		0	0	0	0
		RBT		24	24	0	0
	Brucella abortus / Brucella melitensis	Micr	**Diverse**	18	18	0	0
		ELISA		17	17	0	0
		CFT		0	0	0	0
		RBT	**Diverse**	98	98	0	0

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Brucellosis	*Brucella suis*	Micr	**Swine**	43	43	0	0
		RBT		595	594	0	1
		ELISA		1	0	0	1
		CFT		3	3	0	0
	Brucella ovis (epizootic to be controlled)	ELISA	Sheep	81	78	0	3
	Brucella canis (not counted as an epizootic)	PCR	**Dog**	12	5	0	7
		Cult		14	11	0	3
		LF		51	31	0	20
Bovine Campylo-bacteriosis	*Campylobacter fetus* subspecies *venerealis*	Cult	**Cattle**	826	826	0	0
		PCR		83	83	0	0
Sproadic *Campylobacter* abortion	*Campylobacter fetus* subspecies *fetus*	Cult	**Ruminats**	29	29	0	0
Glanders	*Burkholderia mallei*	CFT	**Horse**	1	1	0	0
		Cult		0	0	0	0

3.1.3 Epizootics to be controlled

Table 4: Number of samples investigated related to epizootics to be controlled

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Leptospirosis	*L.* Australis	MAT	**Cattle**	513	512	1	0
			Dog	63	45	5	13
			Horse	10	8	1	1
			Swine	11	11	0	0
	L. Autumnalis	MAT	**Cattle**	6	6	0	0
			Dog	63	47	10	6
			Horse	10	8	1	1
	L. Ballum	MAT	**Cattle**	96	95	1	0
			Dog	3	2	1	0

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Leptospirosis	*L.* Ballum	MAT	**Swine**	11	11	0	0
	L. Bataviae	MAT	**Cattle**	6	6	0	0
			Dog	63	56	7	0
			Horse	6	5	1	0
	L. Bratislava	MAT	**Cattle**	11	10	1	0
			Dog	62	40	3	19
			Horse	10	7	2	1
			Swine	11	10	1	0
	L. Canicola	MAT	**Cattle**	517	517	0	0
			Dog	63	63	0	0
			Horse	10	10	0	0
			Swine	11	11	0	0
	L. Copenhageni	MAT	**Cattle**	4	4	0	0
			Dog	49	33	5	11
	L. Grippotyphosa	MAT	**Cattle**	517	517	0	0
			Dog	63	57	5	1
			Horse	10	9	1	0
			Swine	11	11	0	0
	L. Hardjo	MAT	**Cattle**	583	521	30	32
			Dog	62	62	0	0
			Horse	6	6	0	0
	L. Icterohaemo-rrhagiae	MAT	**Cattle**	517	517	0	0
			Dog	63	57	4	2
			Horse	10	10	0	0
			Swine	11	11	0	0
	L. Pomona	MAT	**Cattle**	517	512	5	0
			Dog	63	50	6	7
			Horse	10	9	1	0
			Swine	11	11	0	0
	L. Pyrogenes	MAT	**Cattle**	6	6	0	0
			Dog	63	62	1	0
			Horse	6	6	0	0

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Leptospirosis	*L.* Sejroe	MAT	**Cattle**	557	536	21	0
			Dog	21	21	0	0
			Horse	6	6	0	0
	L. Tarasosovi	MAT	**Cattle**	96	96	0	0
			Dog	63	63	0	0
			Horse	6	6	0	0
			Swine	11	11	0	0
	Leptopsira spp. (pathogen)	PCR	**Beaver**	23	12	0	11
			Cattle	52	45	0	7
			Diverse	8	8	0	0
			Dog	4	3	0	1
			Horse	3	3	0	0
			Swine	16	16	0	0
Salmonellosis	*Salmonella* spp.	Cult/ST	**Alpaca**	4	4	0	0
			Ape	10	10	0	0
			Beaver	2	2	0	0
			Bird	107	93	0	14
			Cat	23	23	0	0
			Cattle	188	116	0	72
			Chamois	1	1	0	0
			Chicken	12	12	0	0
			Deer	4	4	0	0
			Dog	59	57	0	2
			Donkey	1	1	0	0
			Elk	5	5	0	0
			Guinea pig	3	3	0	0
			Hare	2	2	0	0
			Goat	17	17	0	0
			Hedgehoge	2	2	0	0
			Horse	64	58	0	6
			Ibex	6	6	0	0
s			**Lizard**	4	3	0	1

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Salmonellosi	*Salmonella* spp.	Cult/ST	**Mouse**	3	3	0	0
			Rabbit	2	2	0	0
			Sheep	20	17	0	3
			Snake	14	10	0	4
			Swine	76	76	0	0
			Tortoise	4	4	0	0
			Wild boar	1	1	0	0
			Zoo animal	59	59	0	0
Contagious equine metritis	*Taylorella equigenitalis*	Cult	**Horse**	131	131	0	0
Enzootic pneumonia in swine	*Mycoplasma hyopneumoniae*	PCR Lung	**Swine**	135	104	0	31
		PCR Nasal swabs		37	33	0	4
		PCR Project		180	133	0	47
		ELISA		239	142	9	88
		ELISA Project		120	78	4	38
Swine actinobacillosis	*Actinobacillus pleuropneumoniae*	Cult/PCR	**Swine**	208	171	0	37
	I BD +II CA, Serotyp 7,12						15
	I BD+II CA+III CA+BD, Serotyp 2						7
	I BD + II CA, Serotyp 2						14
	II CA+IIICA+BD, Serotyp 3						1
		ELISA ApxIV		7	1	1	5

3.1.4 Epizootics to be Monitored

Table 5: Number of samples investigated related to epizootics to be monitored

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Campylobac-teriosis	*C. jejuni / C. coli*	Cult	**Dog**	62	58	0	4
			Cat	23	22	0	1
			Cattle	5	4	0	1
			Diverse	25	0	0	5
Listeriosis	*Listeria monocytogenes*	Cult	**Ruminants**	8	7	0	1
			Primates	8	7	0	1
			Dog	1	0	0	1
Yersiniosis	*Yersinia enterocolitica / Yersinia pseudotuberculosis*	Cult	**Dog**	2	1	0	1
			Cat	3	2	0	1
			Diverse	16	16	0	0
Caseous lymphadenitis in sheep and goats	*Corynebacterium pseudotuberculosis (ovis)*	Cult	**Goat**	2	1	0	1
			Sheep	2	1	0	1
Enzootic abortion in ewes (chlamydiosis)	*Chlamydia abortus*	Micr	**Sheep**	25	20	5	0
		ELISA		85	71	3	11
		PCR		8	0	0	8
		Micr	**Goat**	25	22	3	0
		ELISA		15	12	1	2
		PCR		0	0	0	0
		Micr	**Cattle**	7	7	0	0
		ELISA		11	7	1	3
		PCR		10	10	0	0
		Micr	**Diverse**	0	0	0	0
		ELISA		14	14	0	0
		PCR		2	2	0	0

Epizootic	Agent	Method	Host	Total	Negative	Suspicious	Positive
Psittacosis	*Chlamydia psittaci*	PCR	**Bird**	2	2	0	0
Tularaemia	*Francisella tularensis*	Cult	**Hare**	158	98	0	60
		Cult	**Diverse**	23	23	0	0
Blackleg	*Clostridium chauvoei*	IF	**Ruminant**	16	16	0	0
		Cult		18	18	0	0
Coxiellosis	*Coxiella burnetii*	Micr	**Cattle**	102	100	0	2
		ELISA		19	17	0	2
		PCR		15	9	0	6
		Micr	**Sheep**	32	27	5	0
		ELISA		81	81	0	0
		PCR		9	5	0	4
		Micr	**Goat**	25	22	3	0
		ELISA		10	6	0	4
		PCR		24	16	0	8
		Micr	**Diverse**	0	0	0	0
		ELISA		10	10	0	0
		PCR		3	2	0	1

3.2 Reference Laboratories and Resistance Monitoring

3.2.1 Antimicrobial Resistance Monitoring

Program for food producing animals from Switzerland and meat at retail

The program follows the specifications laid down in the decision 2013/652/EU on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria in Europe. Caecal samples from broilers were collected at slaughter and cultured for indicator *E. coli*, *Campylobacter* spp., extended spectrum beta-lactamases (ESBLs) and carbapenemases producing *E. coli.* Moreover, fresh meat thereof from retail was analysed for ESBLs, carbapenemases producing *E. coli* and methicillin-resistant *Staphylococcus aureus* (MRSA). Isolated strains and all *Salmonella enterica* subspecies *enterica* strains from diagnostics and reference function were tested for antimicrobial susceptibility. Testing was performed by applying the Minimal Inhibitory Concentration (MIC) method.

Results of the antimicrobial resistance monitoring get published in the Swiss antibiotic resistance report, Federal Office of Public Health (FOPH) and Federal Food Safety and Veterinary Office (FSVO). On the European level the results are listed in the European summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food, European Food Safety Authority and European Centre for Disease Prevention and Control.

The numbers of analyses that are part of the 2018 antimicrobial resistance monitoring are displayed in tables 6a to 6f.

Table 6a: Number of analyses on *S. aureus* (MRSA)

Matrix	Number of analyses
broiler meat samples	312
Total	**312**

Table 6b: Number of analyses on ESBL/pAmpC producing *E. coli*

Matrix	Number of analyses
broiler caecal samples	310
broiler meat samples	312
Total	**622**

Table 6c: Number of analyses on carbapenemases producing *E. coli*

Matrix	Number of analyses
broiler caecal samples	310
broiler meat samples	312
Total	**622**

Table 6d: Number of analyses on indicator *E. coli*

Matrix	Number of analyses
briler caecal samples	200
Total	**200**

Table 6e: Number of analyses on *Campylobacter* spp.

Matrix	Number of analyses
broiler caecal samples	650
broiler meat samples	312
Total	**962**

Table 6f: Number of analyses on *Salmonella enterica* subspecies *enterica*

Salmonella serovar	Number of analyses
S. Enteritidis	31
S. Typhimurium	51
S. Typhimurium, monophasic variant	41
other serovars	59
Total	**182**

3.2.2 Confirmation of results from other laboratories (exclusive typing for *Salmonella* spp. and *Actinobacillus pleuropneumoniae*)

Table 7: Number of analyses for confirmation of results from other laboratories (exclusive typing for *Salmonella* spp. and *Actinobacillus pleuropneumoniae*)

Epizootic	Method	Host	Total	Negative	Suspicious	Positive
Anthrax	Micr	**cattle**	0	0	0	0
	Cult		0	0	0	0
Bovine brucellosis	ELISA	**cattle**	10	2	1	7
	RBT		10	10	0	0
	CFT		10	8	0	2
	CULT		2	2	0	0
	PCR		3	3	0	0
Caprine and ovine Brucellosis	ELISA	**sheep/ goat**	1	1	0	0
	RBT		1	1	0	0
	CFT		1	1	0	0
Porcine brucellosis*	ELISA	**swine**	5	3	1	1
	RBT		5	5	0	0
	CFT		5	4	1	0
*farm surveillance	CULT*		15	15	0	0
Canine brucellosis	LF	**dog**	0	0	0	0
	Micr		0	0	0	0
	Cult		0	0	0	0
	Direct PCR		0	0	0	0
Ovine epididymitis (*Brucella ovis*)	ELISA	**sheep**	0	0	0	0
Swine actinobacillosis	ELISA ApxIV	**swine**	0	0	0	0
	Cult		44	2	0	42
Contagious equine Metritis	Cult	**horse**	2	0	1	1
	PCR		0	0	0	0

Epizootic	Method	Host	Total	Negative	Suspicious	Positive
Blackleg	IF	**cattle**	0	0	0	0
	Cult		0	0	0	0
	PCR		0	0	0	0
Campylobacteriosis	ID	**dog**	2	0	0	2
		cattle	3	0	0	3
		diverse	3	0	0	3
Enzootic pneumonia in swine	PCR	**swine**	1	0	0	1
Tularaemia	ID	**hare**	1	0	0	1
Yersiniosis	ID	**fish**	2	1	0	1
*farm surveillance	ID	**Swine***	25	25	0	0
antimicrobial resistance	ID, MIC	**diverse**	63	0	0	63
Coxiellosis	Direct PCR	**sheep**	1	1	0	0

3.2.3 Serotyping of *Salmonella* sp.

Table 8: Number of *Salmonella* spp. isolates for serotyping

Serovar	Host	Number
S. Abony	chicken	1
S. Adelaine	Snake	1
S. Agona	chicken	1
S. Albany	chicken	3
	turkey	7
S. Anatum	chicken	1
S. Beaudesert	lizard	1
S. Benin	snake	1
S. Braenderup	chicken	1
S. Bredeney	lizard	1
S. Caracas	lizard	1
S. Carmel	lizard	1
S. Coeln	chicken	2

Serovar	Host	Number
S. Derby	dog	1
S. Enteritidis	bird	
	cattle	5
	chicken	1
	horse	6
	laying hen	7
	dog	2
	snake	2
S. enterica subsp. arizonae 41: z4,z23: -*	snake	3
S. enterica subsp. arizonae 41: z4,z23,z32: -*	snake	1
S. enterica subsp. arizonae 51: z4,z23: -*	snake	1
S. enterica subsp. diarizonae 53: z10: z35*	snake	1
S. enterica subsp. diarizonae 57 : - : z*	snake	1
S. enterica subsp. diarizonae 42 : r : z53	snake	1
S. enterica subsp. diarizonae 47 : k : 1,5,7	snake	1
S. enterica subsp. diarizonae 61 : - : 1,5,7	sheep	1
S. enterica subsp. diarizonae 61 : k : 1,5,7	sheep	20
S. enterica subsp. diarizonae 53 : k : e,n,z15	chameleon	4
S. enterica subsp. diarizonae 48: l,v : 1,5,7*	chameleon	1
S. enterica subsp. diarizonae 53: k : e,n,x,z15	chameleon	1
S. enterica subsp. diarizonae 48: i : z*	snake	1
S. enterica subsp. enterica 3,10: - : 1,5*	lizard	1
S. enterica subsp. enterica 13,23: i : -	chicken	2
S. enterica subsp. enterica 4,12: c : -	sheep	1
S. enterica subsp. enterica 6,14,24: - : -*	lizard	1
S. enterica subsp. salamae 9,46 : z : z39*	lizard	1
S. enterica subsp. salamae 42 : b : e,n,x,z15*	lizard	2
S. enterica subsp. salamae 58:c:z6	lizard	1
S. Florida	snake	1
S. Idikan	chicken	1
S. Kisaware	lizard	1
S. Kortrijk	lizard	1

Serovar	Host	Number
S. Livingstone	laying hen	1
	chicken	1
S. Montevideo	lizard	4
S. Muenchen	snake	1
S. Napoli	horse	1
S. Newport	horse	1
S. Nigeria	dog	1
S. Ohlstedt	lizard	1
S. Oranienburg	tortoise	1
	dog	3
S. Othmarschen	lizard	1
S. Parathyphi B	snake	1
S. Runby	lizard	1
S. Sandiego	snake	1
S. Stourbrigde	horse	2
S. Tennessee	chicken	11
S. Typhimurium	cattle	85
	chicken	6
	laying hen	7
	rabbit	5
	sheep	1
	bird	4
	dog	1
	swine	1
	turkey	1
	horse	1
S. Typhimurium, monophasic variant (4,12 : i : -)	cattle	19
	laying hen	1
	chicken	17
	bird	1
	dog	4
S. Veneziana	dog	1

Serovar	Host	Number
S. Welikade	chicken	1
No Salmonella		3
	Total	300

3.2.4 Swine actinobacillosis: PCR based identification of *Actinobacillus pleuropneumoniae* by *apx* toxin gene typing and *cps2* gene detection

Table 9: Number of *Actinobacillus pleuropneumoniae* (APP) isolates for typing received from other laboratories

Biovar	apx group	Serotype	Number
Biovar I	apx group: I BD + II CA	7,12	21
Biovar I	apx group: I BD + II CA + III CA + BD *cps*2 gene positive	2	8
Biovar II	apx group: I BD + II CA *cps*2 gene positive	2	13
No APP	-	-	2
Total			**44**

3.2.5 Leptospirosis Diagnostics for Humans

Table 10: Number of samples investigated related to humane medicine

Zoonosis	Agent	Method	Host	Total	Negative	Suspicious	Positive
Leptospirosis	*L.* Andaman	MAT	**Human**	5	3	2	0
	L. Australis			8	7	1	0
	L. Autumnalis			8	8	0	0
	L. Ballum			6	6	0	0
	L. Bataviae			7	4	3	0
	L. Bratislava			7	7	0	0
	L. Canicola			7	7	0	0
	L. Celledoni			5	5	0	0
	L. Copenhageni			8	8	0	0
	L. Cynopetri			5	5	0	0
	L. Grippotyphosa			8	6	2	0
	L. Hardjo			7	3	2	2

Zoonosis	Agent	Method	Host	Total	Negative	Suspicious	Positive
	L. Hebdomalis			5	4	1	0
	L. Icterohaemo-rrhagiae			8	8	0	0
	L. Javanica			5	4	1	0
	L. Panama			5	5	0	0
	L. Patoc			5	0	3	2
	L. Pomona			8	8	0	0
	L. Pyrogenes			8	8	0	0
	L. Sejroe			7	3	3	1
	L. Shermani			5	0	3	2
	L. Tarassovi			7	6	1	0
		PCR		1	1	0	0

3.2.6 Organisation of Proficiency Testing for approved laboratories

As a Swiss national reference laboratory for brucellosis, salmonellosis and antimicrobial resistance the ZOBA is responsible for the diagnostic quality of the approved laboratories in Switzerland. For this purpose the ZOBA organized proficiency testings for these laboratories, which are mandatory for the approval by the Federal Food Safety and Veterinary Office. The proficiency testings conducted in 2018 are listed in Table 11.

Table 11: Proficiency testings for approved laboratories organised by the ZOBA in 2018

Target	Method	Number of samples	Number of laboratories
Brucellosis	serology	10	10
Antimicrobial susceptibility testing	diverse	6	10
Salmonellosis	Questionnaire on serotyping methods	-	8

3.3 Research Activities

3.3.1 Swiss Antibiotic Resistance Report 2018. Usage of Antibiotics and Occurrence of Antibiotic Resistance in Bacteria from Humans and Animals in Switzerland.

Publication: Swiss Antibiotic resistance report 2018 Federal Office of Public Health and Federal Food Safety and Veterinary Office. November 2018. FOPH publication number: 2018-OEG-87.

Main authors: Dagmar Heim, Federal Food Safety and Veterinary Office, Andreas Kronenberg, Swiss Centre for Antibiotic Resistance, Institute for Infectious Diseases, University of Bern, Gudrun Overesch, Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance, Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern, Catherine Plüss-Suard, Hospital Preventive Medicine, University Hospital of Lausanne, Gertraud Schüpbach, Veterinary Public Health Institute, Vetsuisse Faculty University of Bern

3.3.2 Salmonella enterica subspecies diarizonae serovar 61:(k):1,5,(7) as cause of caprine abortion.

Publication: Schnydrig, P; Overesch, G; Regli, W; Bee, A; Rodriguez-Campos, S. 2018.
Small ruminant research, **166**, S. 78-82.

Collaborators: labor-zentral.ch AG, Stationsweg 3, 6232 Geuensee, Switzerland, Service de la Sécurité Alimentaire et des Affaires Vétérinaires, Impasse de la Colline 4, 1762 Givisiez, Switzerland

Abstract: *Salmonella enterica* subsp. *diarizonae* (IIIb) 61:(k):1,5,(7) is commonly found in sheep and is considered to be host-adapted to this species, although it can lead to abortion, stillbirth, diarrhea, chronic proliferative rhinitis and orchitis/epididymitis. Infections with S. IIIb 61:(k):1,5,(7) in humans were also reported, although its zoonotic potential is generally considered low (Sörén et al., 2015). This study includes four strains from ovine abortions and one strain from abortion material from a goat. To our knowledge this is the first report of *Salmonella enterica* subsp. *diarizonae* 61:(k):1,5,(7) as cause of caprine abortion. The strains originating from abortion material and strains from different sample material including feces, nasal and carcass swabs from sheep were characterized by pulsed-field gel electrophoresis (PFGE) and antimicrobial susceptibility testing. Our study could not reveal a common pulsotype of the strains isolated from abortion. The clustering of the clinical strains with isolates from normal microbiota suggests a role of S. IIIb 61:(k):1,5,(7) as a real opportunistic pathogen.Antimicrobial susceptibility testing showed no phenotypic resistance for any of the strains.

3.3.3 Otitis in a cat associated with *Corynebacterium provencense*.

Publication: Kittl S, Brodard I, Rychener L, Jores J, Roosje P, Gobeli Brawand S BMC Vet Res. 2018 Jun 25;14(1):200. doi: 10.1186/s12917-018-1526-9
Collaborators: Division of Clinical Dermatology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bremgartenstrasse 109a, CH-3001, Bern, Switzerland
Abstract: BACKGROUND: The role of corynebacteria in canine and feline otitis has not beeninvestigated in detail; however, members of this genus are increasinglyrecognized as pathogens of otitis in both human and veterinary medicine.CASE PRESENTATION: Here we

report the first case of feline otitis associated withthe recently described species Corynebacterium provencense. A seven-month old catpresented with a head tilt and ataxia was diagnosed with peripheral vestibularsyndrome associated with an otitis media/interna. This took place 6 weeks afterresection of a polyp, having initially shown a full recovery with topicalofloxacin and glucocorticoid treatment. Bacteriology of an ear swab yielded apure culture of corynebacteria, which could not be identified at the specieslevel using routine methods. However, the 16S rRNA gene sequence was 100% identical to the recently published novel corynebacterium species,Corynebacterium provencense. Whole genome sequencing of the cat isolate andcalculation of average nucleotide identity (99.1%) confirmed this finding. Thecat isolate was found to contain additional presumptive iron acquisition genesthat are likely to encode virulence factors. Furthermore, the strain testedresistant to clindamycin, penicillin and ciprofloxacin. The cat was subsequently treated with chloramphenicol, which lead to clinical improvement.CONCLUSION: Corynebacteria from otitis cases are not routinely identified at the species level and not tested for antimicrobial susceptibility in veterinarylaboratories, as they are not considered major pathogens. This may lead tounderreporting of this genus or animals being treated with inappropriateantimicrobials since corynebacteria are often resistant to multiple drugs.

4 Teaching Obligations

4.1 Bacteriology Lecture Series

General Bacteriology and Mycology:	26 x 45 min
Clinical Bacteriology and Mycology:	26 x 45 min
Berufskunde:	1 x 45 min

4.2 Organ Specific Lectures

Blood/Laboratory/Immune system:	1 x 45 min
Skin and Thermoregulation:	1 x 45 min

4.3 Clinical Topics

Population Medicine:	8 x 45 min

4.4 Hands on Courses

Practical Course in Bacteriology:	48 x 45 min
Practical Course in Microbial and Immunological Diagnostics:	56 x 45 min

5 Publications

5.1 Peer-Reviewed Publications

1. Aguilar-Bultet L, Nicholson P, Rychener L, Dreyer M, Gozel B, Origgi FC, Oevermann A, Frey J, Falquet L. 2018. Genetic Separation of *Listeria monocytogenes* Causing Central Nervous System Infections in Animals. Front Cell Infect Microbiol 8:20.
2. Aye R, Weldearegay YB, Lutta HO, Chuma F, Pich A, Jores J, Meens J, Naessens J. 2018. Identification of targets of monoclonal antibodies that inhibit adhesion and growth in *Mycoplasma mycoides* subspecies *mycoides*. Vet Immunol Immunopathol 204:11-18.
3. Bentahir M, Ambroise J, Delcorps C, Pilo P, Gala JL. 2018. Sensitive and Specific Recombinase Polymerase Amplification Assays for Fast Screening, Detection, and Identification of *Bacillus anthracis* in a Field Setting. Appl Environ Microbiol 84.
4. Bernasconi OJ, Dona V, Pires J, Kuenzli E, Hatz C, Luzzaro F, Perreten V, Endimiani A. 2018. Deciphering the complete deletion of the *mgrB* locus in an unusual colistin-resistant *Klebsiella pneumoniae* isolate colonising the gut of a traveller returning from India. Int J Antimicrob Agents 51:529-531.
5. Burgi N, Josi C, Burki S, Schweizer M, Pilo P. 2018. *Mycoplasma bovis* co-infection with bovine viral diarrhea virus in bovine macrophages. Vet Res 49:2.
6. Chanchaithong P, Prapasarakul N, Sirisopit Mehl N, Suanpairintr N, Teankum K, Collaud A, Endimiani A, Perreten V. 2018. Extensively drug-resistant community-acquired *Acinetobacter baumannii* sequence type 2 in a dog with urinary tract infection in Thailand. J Glob Antimicrob Resist 13:33-34.
7. Clement M, Budel T, Bernasconi OJ, Principe L, Perreten V, Luzzaro F, Endimiani A. 2018. The EDTA-based disk-combination tests are unreliable for the detection of *MCR*-mediated colistin-resistance in Enterobacteriaceae. J Microbiol Methods 153:31-34.
8. De Luca S, Nicholson P, Magistrali CF, Garcia-Martin AB, Rychener L, Zeeh F, Frey J, Perreten V. 2018. Transposon-associated lincosamide resistance *lnu*(C) gene identified in *Brachyspira hyodysenteriae* ST83. Vet Microbiol 214:51-55.
9. Dona V, Perreten V. 2018. Comparative Genomics of the First and Complete Genome of "*Actinobacillus porcitonsillarum*" Supports the Novel Species Hypothesis. Int J Genomics 2018:5261719.
10. Egli A, Blanc DS, Greub G, Keller PM, Lazarevic V, Lebrand A, Leib S, Neher RA, Perreten V, Ramette A, Schrenzel J, Stephan R, Wagner K, Wuethrich D, Xenarios I. 2018. Improving the quality and workflow of bacterial genome sequencing and analysis: paving the way for a Switzerland-wide molecular epidemiological surveillance platform. Swiss Med Wkly 148:w14693.

11. Elad D, Blum SE, Perreten V, Fleker M, Avni Z, Weisbelith L. 2018. Emergence and prevalence decline of a phenotypically multidrug-resistant *Staphylococcus pseudintermedius* in Israel. Israel Journal of Veterinary Medicine 73:14-18.
12. Fouche N, Gerber V, Thomann A, Perreten V. 2018. Antimicrobial susceptibility patterns of blood culture isolates from foals in Switzerland. Schweiz Arch Tierheilkd 160:665-671.
13. Garcia-Martin AB, Perreten V, Rossano A, Schmitt S, Nathues H, Zeeh F. 2018. Predominance of a macrolide-lincosamide-resistant *Brachyspira hyodysenteriae* of sequence type 196 in Swiss pig herds. Vet Microbiol 226:97-102.
14. Gobeli Brawand S, Rychener L, Schwendener S, Pantucek R, Perreten V. 2018. Complete Genome Sequence of the Type Strain of *Macrococcus canis*. Genome Announc 6.
15. Greber D, Locher I, Kuhnert P, Butty MA, Holdener K, Frey J, Schupbach-Regula G, Steiner A. 2018. Pooling of interdigital swab samples for PCR detection of virulent *Dichelobacter nodosus*. J Vet Diagn Invest 30:205-210.
16. Guccione J, Della Valle G, Carcasole C, Kuhnert P, Alsaaod M. 2018. Detection of *Treponema pedis* associated with digital dermatitis in Mediterranean buffalo (*Bubalus bubalis*). Vet Rec Case Reports 6:e000674.
17. Josi C, Burki S, Stojiljkovic A, Wellnitz O, Stoffel MH, Pilo P. 2018. Bovine Epithelial in vitro Infection Models for *Mycoplasma bovis*. Front Cell Infect Microbiol 8:329.
18. Kittl S, Brodard I, Rychener L, Jores J, Roosje P, Gobeli Brawand S. 2018. Otitis in a cat associated with *Corynebacterium provencense*. BMC Vet Res 14:200.
19. Locher I, Giger L, Frosth S, Kuhnert P, Steiner A. 2018. Potential transmission routes of *Dichelobacter nodosus*. Vet Microbiol 218:20-24.
20. Machado RAR, Wuthrich D, Kuhnert P, Arce CCM, Thonen L, Ruiz C, Zhang X, Robert CAM, Karimi J, Kamali S, Ma J, Bruggmann R, Erb M. 2018. Whole-genome-based revisit of *Photorhabdus* phylogeny: proposal for the elevation of most *Photorhabdus* subspecies to the species level and description of one novel species *Photorhabdus bodei* sp. nov., and one novel subspecies *Photorhabdus laumondii* subsp. *clarkei* subsp. nov. Int J Syst Evol Microbiol 68:2664-2681.
21. Maes D, Sibila M, Kuhnert P, Segales J, Haesebrouck F, Pieters M. 2018. Update on *Mycoplasma hyopneumoniae* infections in pigs: Knowledge gaps for improved disease control. Transbound Emerg Dis 65 Suppl 1:110-124.
22. Massacci FR, De Luca S, Cucco L, Tentellini M, Perreten V, Pezzotti G, Magistrali CF. 2018. Multiresistant *Brachyspira hyodysenteriae* shedding by pigs during the fattening period. Vet Rec 183:264.
23. Pilo P. 2018. Phylogenetic Lineages of *Francisella tularensis* in Animals. Front Cell Infect Microbiol 8:258.

24. Pilo P, Frey J. 2018. Pathogenicity, population genetics and dissemination of *Bacillus anthracis*. Infect Genet Evol 64:115-125.
25. Pires J, Kuenzli E, Hauser C, Tinguely R, Kasraian S, Atkinson A, Rauch A, Furrer H, Perreten V, Marschall J, Hatz C, Endimiani A. 2018. Intestinal colonisation with extended-spectrum cephalosporin-resistant Enterobacteriaceae in different populations in Switzerland: prevalence, risk factors and molecular features. J Glob Antimicrob Resist 12:17-19.
26. Sartori C, Perreten V, Ivanovic I, Hardi-Landerer MC, Graber HU. 2018. Short communication: Lack of intramammary niche recolonization during a sanitation program for the contagious mastitis pathogen *Staphylococcus aureus* genotype B. J Dairy Sci 101:8296-8300.
27. Schwendener S, Perreten V. 2018. The integrase of the *Macrococcus caseolyticus* resistance island *mecD* (McRImecD) inserts DNA site-specifically into *Staphylococcus* and *Bacillus* chromosomes. Mol Microbiol 110:455-468.
28. Vidal S, Brandt BW, Dettwiler M, Abril C, Bressan J, Greub G, Frey CF, Perreten V, Rodriguez-Campos S. 2018. Limited added value of fungal ITS amplicon sequencing in the study of bovine abortion. Heliyon 4:e00915.
29. Wittwer M, Altpeter E, Pilo P, Gygli SM, Beuret C, Foucault F, Ackermann-Gaumann R, Karrer U, Jacob D, Grunow R, Schurch N. 2018. Population Genomics of *Francisella tularensis* subsp. *holarctica* and its Implication on the Eco-Epidemiology of Tularemia in Switzerland. Front Cell Infect Microbiol 8:89.
30. Worthing KA, Schwendener S, Perreten V, Saputra S, Coombs GW, Pang S, Davies MR, Abraham S, Trott DJ, Norris JM. 2018. Characterization of Staphylococcal Cassette Chromosome *mec* Elements from Methicillin-Resistant *Staphylococcus pseudintermedius* Infections in Australian Animals. mSphere 3.
31. Zeeh F, De Luca S, Nicholson P, Grutzner N, Nathues C, Perreten V, Nathues H. 2018. *Brachyspira hyodysenteriae* detection in the large intestine of slaughtered pigs. J Vet Diagn Invest 30:56-63.
32. Zeeh F, Klausmann S, Masserey Y, Nathues H, Perreten V, Rohde J. 2018. Isolation of *Brachyspira hyodysenteriae* from a crow (*Corvus corone*) in close proximity to commercial pigs. Vet J 236:111-112.

5.2 Book Chapters

- N/A

5.3 Other Publications

- Swiss Antibiotic resistance report 2018 Federal Office of Public Health and Federal Food Safety and Veterinary Office. November 2018. FOPH publication number: 2018-OEG-87.

  Main authors: Dagmar Heim, Federal Food Safety and Veterinary Office, Andreas Kronenberg, Swiss Centre for Antibiotic Resistance, Institute for Infectious Diseases, University of Bern, Gudrun Overesch, Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance, Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern, Catherine Plüss-Suard, Hospital Preventive Medicine, University Hospital of Lausanne, Gertraud Schüpbach, Veterinary Public Health Institute, Vetsuisse Faculty University of Bern

- Schlussbericht zum Pilotprojekt über die Überwachung von Antibiotikaresistenzen bei tierpathogenen Erregern -Version für Tierärzte –

  Main authors: Dagmar Heim, Federal Food Safety and Veterinary Office, and Gudrun Overesch, Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance, Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern

5.4 Press Releases and Broadcasting

- **Schweizer Bauern spritzen rekordmässig Antibiotika.**
  Yves Demuth. Beobachter 22/2018, October 26th, 2018

- **L'angoisse d'être intoxiqué**
  Sandrine Hochstrasser. La Liberté, August 27th 2018

6 Graduations and Visting Scientists

6.1 PhD Degrees

Name of student: Sara Vidal

Graduate School: Cellular and Biomedical Sciences, University of Bern, Switzerland

Title of Thesis: Broad-spectrum analyses of bovine abortion: deciphering neglected agents

Supervisors: Sabrina Rodriguez Campos and Vincent Perreten

Abstract: Abortion in ruminants has a significant economic impact in the livestock industry and can be caused by important zoonotic agents requiring prompt diagnosis of possible causes. The etiology of abortion is very complex and the majority of abortions are not epizootic but sporadic. Yet, few infectious agents are examined in routine abortion diagnosis. In microbiome research, next generation sequencing (NGS) has become a valuable tool in microbial community studies. To improve the knowledge of the bacterial and fungal community present in bovine abortion this PhD project explored novel technologies: i) application of Illumina MiSeq bacterial 16S rRNA gene and fungal ITS2 sequencing technology in abortion material, ii) comparison of novel molecular diagnostic methods such as real-time PCR with methods applied in routine diagnostics. Amplicon sequencing of the 16S rRNA gene revealed possible abortive agents that were not detected in the routine diagnostic approach. Increased knowledge of the microbiota involved in abortion offered new perspectives in diagnosis, e.g. the implication of previously undiagnosed bacteria such as Pseudomonas spp. In contrast to 16S rRNA gene amplicon sequencing, the use of fungal ITS2 amplicon sequencing did not provide any additional information in comparison with classical methods and could lead to false interpretation of the true clinical significance of the presence of a fungal organism in bovine abortion samples. We could corroborate that methods applied in routine diagnostics such as Stamp's modified Ziehl-Neelsen staining underestimate the presence of zoonotic bacterial species and that the implemented real-time PCRs had high sensitivity for the detection of different pathogens in abortion material. Thus, we recommend an extended workflow including molecular analysis for routine abortion diagnostics to enhance its diagnostic value and avoid the underestimation of the discussed agents. Overall, our results highlight that 16S rRNA gene amplicon sequencing is a useful tool for the detection of emerging pathogens and that the clarification rate of bovine abortion can be raised significantly by increasing the spectrum of analyzed pathogens and including molecular techniques.

6.2 Dr. vet. med. Degrees

Name of student: Ana C Hausherr

Title of Thesis: Resistance to antibiotics and quaternary ammonium compounds of *Escherichia coli* from calves at the beginning of the mast period in Switzerland.

Supervisor: Vincent Perreten

Abstract: Susceptibility to antibiotics and quaternary ammonium compounds (QAC) was determined for 100 *E. coli* from calves entering rearing in Switzerland, revealing that 36% of the isolates were susceptible to the antimicrobials tested and 48% were susceptible to QAC. All isolates were susceptible to colistin, tigecycline and meropenem. Resistance to more than 3 antibiotics was found in 59% of the isolates. Isolates exhibited resistance to tetracycline (59%) associated with the presence of *tet* genes (*tet*(A), (B), (E), (G)), to sulfonamides (63%) (*sul1*, *sul2*, *sul3*), β-lactams (58%) (*bla*$_{TEM-1}$), trimethoprim (34%) (*dfrA*), gentamicin (29%) (*ant(2")-Ia*, *aac(3)-VIa*, *aac(3)IV*, *aac(3)-IV; aac(3)-IIc*), streptomycin (46%) (*strA*, *strB*, *aadA*) and ceftazidime (1%) (*bla*$_{CTX-M-9}$ (ESBL)). Mutations in GyrA (S83L) and ParC (S80I) were found in fluoroquinolone resistant isolates (8%). All isolates were susceptible to colistin, tigecycline and meropenem. No association between the presence of decreased susceptibility to ADBAC and *qac* genes was observed. Genetic diversity between isolates was determined using repetitive palindromic PCR (*rep*-PCR) revealing a genetically diverse *E. coli* population. In conclusion, antibiotic and QAC resistant *E. coli* are present in the gut of young calves at the beginning of the rearing period, emphasizing the need of appropriate and reduced use of antibiotics and QAC-containing disinfectants in order to limit further selection and maintenance of these bacteria during rearing period.

Name of student: Susanne Hofer

Title of Thesis: Contribution towards the establishment of Clinical Breakpoints (CBPs) for veterinarian antimicrobials: Distribution of Minimal Inhibitory Concentrations (MICs) of antimicrobials in Swiss livestock pathogens.

Supervisor: Gudrun Overesch

Abstract: Antimicrobial Susceptibility Testing (AST) is crucial for a targeted antimicrobial therapy and its interpretation is based on Clinical Breakpoints (CBPs). Determination of Minimal Inhibitory Concentrations (MICs) for a bacterial pathogen represents an important step towards setting CBPs. Since MIC data are still scarce for some relevant veterinary pathogens, we determined MICs using broth microdilution for a number of bacterial livestock pathogens (*Streptococcus (S.) uberis* (n=97), *S. suis* (n=33), *Trueperella (T.) pyogenes* (n=78), *Pasteurella (P.) multocida* (n=81) and *Mannheimia (M.) haemolytica* (n=37)) previously collected from clinical samples. The distributions of MICs contributed to the identification of Wildtype (WT) versus non-Wildtype (non-WT) phenotype of these pathogens. They permit to see if non-WT populations were present among these bacteria in Switzerland indicating possible emergence of resistance. These data constitute a basis for the establishment of Epidemiological Cut-Off values (ECOFFs) by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for specific antibiotics used in veterinary medicine.

6.3 Master Degrees

Name of student: Simona Gerber

Title of Thesis: Generation of porcine *Mycoplasma* mutant libraries to reveal potential virulence determinants and study host-pathogen interactions.

Supervisors: Peter Kuhnert and Bettina Trüeb

Abstract: Enzootic pneumonia is a respiratory disease in pigs mainly caused *by Mycoplasma hyopneumoniae* infection leading to significant economic losses to swine producers worldwide. To date, there is little known about the molecular pathogenesis of the disease due to difficulties of genetic manipulation of mycoplasmas and the complicated relationship between the pathogens and their hosts. No commercial vaccines are available that are able to successfully prevent colonization of the respiratory tract with *M. hyopneumoniae* or effectively eliminate infection from the organism. *Mycoplasma hyorhinis* is often found in the upper respiratory tract and tonsils of healthy pigs and despite being seen as a commensal inhabitant of the airways, *M. hyorhinis* is considered to facilitate and exacerbate the development of various diseases including mycoplasmal arthritis. In order to design and establish more effective vaccines against porcine mycoplasmas, a better understanding of their pathogenicity is required. In this study, we hypothesized that non-essential genes may encode potential virulence determinants in both *M. hyorhinis and M. hyopneumoniae*. Our study aimed at identifying such genes using PEG-mediated global transposon mutagenesis. Mutant libraries were successfully generated for both *M. hyorhinis* strain JF5820 and *M. hyopneumoniae* strain F7.2C. Transposon-sequencing (Tn-seq) was performed using semi-arbitrary primers and deep amplicon sequencing by Illumina. In this study, the Tn-seq dataset was analyzed for *M. hyorhinis* strain JF5820 revealing essential and non-essential genes. Genes coding for the acid phosphatase, aspartate-ammonia ligase, serine/threonine phosphatase, variable lipoproteins, immunoglobulin A1 protease, sialic acid metabolism, type I restriction and modification system and glycosyltransferase were shown be non-essential and could be potential virulence determinants. As such, they could be candidates for the generation of an attenuated live vaccine against *M. hyorhinis*. Furthermore, the generated mutant library of *M. hyorhinis* JF5820 was screened for the specific MIB-MIP-Tn-mutant by Western blot. A preexisting mutant library of *M. hyopneumoniae* strain F7.2C was screened for the specific *mnuA*- and *mmsA*-Tn-mutants by PCR. The mutants of interest are believed to be involved in the pathogenicity of porcine mycoplasmas and are candidates for vaccines. Additionally, Multilocus sequence typing was used to confirm the sequence type of *M. hyorhinis* strain JF5820.

6.4 Visiting Scientists

Name of student: Dr. Cristina Pesca (Istituto Zooprofilattico Sperimentale Umbria and Marche, Perugia, Italy)

Name of Research Project: Isolation and molecular serotyping of *Dichelobacter nodosus* samples from Swiss infected flocks

Supervisor: Peter Kuhnert and Isabelle Brodard

Name of student: Nathita Phumthanakorn (Chulalongkorn University, Bangkok, Thailand)

Name of Research Project: Whole genome sequencing and analysis of *Staphylococcus pseudintermedius* strains from human and dog origins.

Supervisor: Vincent Perreten and Sybille Schwendener

Name of student: Rosa Elena Hernández Fillor (National Centre for Animal and Plant Health (CENSA), San José de las Lajas, Mayabeque, Cuba).

Name of Research Project: Characterization of 3rd generation cephalosporin-resistant *Escherichia coli* isolated from pigs in Cuba using Next Generation Sequencing

Supervisor: Vincent Perreten

7 Scientific Meetings Organized, Keynotes given and Grants Awarded

7.1 Scientific Meetings Organized by IVB Staff

- Jörg Jores, 31st January – 1st February 2018, GALVmed & Bill and Melinda Gates foundation (BMGF) & University of Bern (UoB), Workshop 'Contagious Bovine Pleuropneumonia and Contagious Caprine Pleuropneumonia: an update on the current knowledge base'
- Jörg Jores, BD seminar, Bern 20th November 2018, Scientific committee

7.2 Keynote/Invited Lectures Given by IVB Staff

- Jörg Jores, 16th June 2018, Title: "Epizootic control in the Horn of Africa", Annual Meeting of VSF Switzerland, Goldau, Switzerland
- Jörg Jores, 20th November 2018, Bern, Switzerland, Title: "Two recent Swiss case reports of zoonotic pathogens: *Bacillus antracis* and *Leptospira* spp. infections
- Gudrun Overesch, 1th February 2018 Rothenburg, Switzerland. Bakterielle Zoonosen, Vorkommen und aktuelle Bedrohungslage in der Schweiz. Fortbildungveranstaltung der Gesellschaft Zentral Scheizerischer Tierärzte (GZST)
- Gudrun Overesch, 09th October, Uppsala, Sweden, Title: "Monitoring of Swiss broiler meat with a qPCR for the detection of *Campylobacter jejuni/coli*", Annual Workshop of the European Reference Laboratory for Campylobacter
- Gudrun Overesch, 25th October 2018, Bern, Switzerland, Title: "Swiss Monitoring of antimicrobial resistance in veterinary pathogens from cattle, swine, small ruminants, horses, dogs and cats", Annual Meeting of Veterinary Diagnostic Laboratories, Federal Food Safety and Veterinary Office
- Gudrun Overesch, 09th November 2018, Parma, Italy, Title: "The monitoring of MRSA in pigs in Switzerland: an update", Scientific Network for Zoonoses Monitoring Data, 8th specific meeting on Antimicrobial Resistance data reporting by the European Food Safety Authority (EFSA)
- Peter Kuhnert, 8th October 2018, Title: "Current and future methods for identifying *Pasteurellaceae*". Prato Conference on Animal Pathogens (MedVet Pathogens), Prato, Italy
- Peter Kuhnert, 10th November 2018, Title: "Zoonotic *Campylobacter* in Switzerland: what we learned over 10 years" (invited speaker for the Geoff Simmons Memorial Lecture). Annual Meeting of the Australian Society for Microbiology QLD Branch (MiM2018), Sandstone Point, QLD, Australia
- Vincent Perreten, 13th September 2018 Rothenburg, Switzerland. Antibiotikaresistenzen: Grundlagen der Resistenzentstehung, Verbreitung und –Messung. Fortbildungveranstaltung der Gesellschaft Zentral Scheizerischer Tierärzte (GZST)

- Vincent Perreten, 14th June, 2018. Discovery of Novel Antibiotic Resistance Genes using Next-Generation Sequencing. The University of Tennessee, College of Veterinary Medicine, Knoxville, TN.

7.3 Competitive Grants Awarded

- Donor: Swiss National Science Foundation (SNSF). Whole Genome and Plasmid Sequencing for MDR Enterobacteriaceae Simultaneously Isolated from Multiple Human and Non-Human Settings: Deciphering Impact, Risks, and Dynamics for Resistance Transmission and Spread. Duration: 03.2018 - 02.2021. Principal Investigator: Andrea Endimiani (Institute for Infectious Diseases, University of Bern); co-applicants: Vincent Perreten (Institute of Vterinary Bacteriology), Alban Ramette (Institute for Infectious Diseases, University of Bern).
- Donor: Swiss National Science Foundation (SNSF). Development of a Swiss surveillance database for molecular epidemiology of multi-drug resistant pathogens. Duration: 03.2018 - 02.2021. Adrian Egli (Departement Biomedizin Universität Basel); co-applicants: Gilbert Greub (Institut de Microbiologie Faculté de Biologie et Médecine CHUV/Université de Lausanne); Aitana Lebrand (SIB Swiss Institute of Bioinformatics Clinical Bioinformatics); Blanc Dominique (Service de Médecine Préventive Hospitalière CHUV); Neher Richard (Biozentrum der Universität Basel); Perreten Vincent (Institut für Veterinär-Bakteriologie Vetsuisse-Fakultät Universität Bern) ; Schrenzel Jacques (Laboratoire de Recherche Génomique Service des Maladies Infectieuses Hôpital Cantonal – HUG)
- Donor: Federal Food Safety and Veterinary Office (FSVO). Prevalence and identification of critical points for transmission of multidrug-resistant bacteria in small animal clinics - towards evidence-based guidelines for good hygiene practice. Duration: 04.2018-9/2019. Principal Investigators: Simone Schuller (Department of Clinical Veterinary Medicine, University of Bern) and Barbara Willi (Clinic for Small Animal Internal Medicine, University of Zurich); Co-applicants: Vincent Perreten, Stefanie Gobeli (Institute of Veterinary Bacteriology, University of Bern); Andrea Endimiani (Institute for Infectious Diseases, University of Bern); Stefan Kuster (Division of Infectious Diseases and Hospital Epidemiology, University and University Hospital of Zurich)

7.4 Other funding

- Donor: Huvepharma; Project title: "Determination of minimal inhibitory concentrations (MICs) of relevant pathogens for the establishment of epidemiological cut offs (ecoffs) according to EUCAST", Duration: 10//2018-9/2020; Principal Investigator: Jörg Jores, Institute of Veterinary Bacteriology, University of Bern (Switzerland)

8 Organization Chart (Organigram)