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January – December 2022



Graduate School of Veterinary Medicine Rakuno Gakuen University







2022年(1月~12月)の獣医学研究科英文業績集の発刊にあたって

酪農学園大学大学院 獣医学研究科長 桐澤 力雄

獣医学研究科では獣医学群教員が 1 年間に公表した英語論文を冊子体にまとめ、各教員の自己点検や研究の質保証、並びに関係各位に獣医学群教員の研究状況を紹介する目的で、2002年より業績集を刊行しています。

2022年の筆頭著者(FA)及び責任著者(CA)の論文合計は68報でした。過去5年間では、2021年:83報、2020年:72報、2019年:54報、2018年:54報、2017年:48報、となっており、昨年より15報減少しました。著しく行動制限のかかったCOVID・19の影響が出たものと考えられます。近5年間にFA/CA論文のない教員が9名いました(教授:2名、准教授:4名、講師:3名)。代表的な競争的資金である科研費の学群教員の申請状況をみると、2023年度:49名、2022年度:51名、2021年度:43名、2020年度:40名、2019年度:36名、2018年度:34名、2017年度:38名でした。2023年度の申請率は応募可能な学群教員が60名でしたので約82%(昨年は約89%、一昨年約83%)となり、昨年より若干申請率が低下しました。しかし、本学全体の科研費採択件数をみると、2020年:31件、2021年:37件、2022年:48件で、増加傾向にあり、全国私立大学の配分額の順位も2020年:133位、2021年:129位、2022年:119位(配分された585大学中)と上昇傾向にあります。教員個々の研究レベルの高まりが反映されているものと推察しますが、本学においては、研究に必要な高額機器・備品の更新や投資がほとんどなされていない現状、ならびに学群で進めているEAEVE対応の教育負担増を見ると、今後の研究の進展が憂慮されます。

科学技術指標 2022 によると自然科学系の科学論文数(2018 - 2020 年平均)の順位は昨年から順位を一つ下げ、中国、アメリカ、ドイツ、インド、そして日本となっております。日本は 10 年前が 3 位で論文シェアは 6.0 %ありましたが、今回はシェアが 3.9%に低下しています。Top10%補正論文数も 10 年前の 6 位から 12 位に後退しています(昨年は 10位)。シェアも 10 年前の 4.0%から 2.2%に低下し、わが国の長期にわたる凋落傾向が読み取れます。獣医学研究科の論文数も、その潮流に流されないように最大限の工夫をする必要があります。その一方で、研究費が潤沢な中国は Top1%補正論文数においても、米国を抜いて初めて世界第 1 位となり、中国は世界の論文や注目度の高い論文におけるリード度でも世界第 1 位となっています。

2022 年度の獣医学専攻博士課程の在籍者総数は 27 名 {社会人大学院生:14名、外国人:5名(中国:2名、台湾:1名、カンボジア:1名、タイ:1名)} で、今年度の修了認定者は 5 名です。獣医保健看護学専攻修士課程の在籍者総数は 4 名で、今年度の修了認定者は 2 名です。今年度も大学院博士課程に第一種奨学生採用時返還免除内定候補者枠が、4 年連

続で1名付与されました。

2019 年度から始動した「One Health フロンティア卓越大学院」には、獣医学研究科から 3 年生 2 名が登録し、北大や帯広畜産大学の大学院生とともに講義・実習を履修しています。来年度から、獣医学研究科では独立行政法人国際協力機構(JICA)の長期研修コースによる外国人留学生の受け入れを開始し、現在、4 名の出願が見込まれています。国際化を目指している獣医学群において、外国人留学生が増えることは日本人学生に大きな刺激を与えることが期待されます。

最後に関係各位には本業績集をご高覧いただき、教員個々の研究内容などから共同研究、 さらには広範な研究体制の構築等へとご高配いただけることを願っております。今後とも、 獣医学研究科の教育・研究活動がさらに発展するよう、ご指導ご鞭撻をよろしくお願い申し 上げます。

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Tongue worm (Subclass: Pentastomida) infection and treatment in two pet reptiles—a case report.

Takaki, Y., Irie, T., Takami, Y., <u>Asakawa, M.</u> and Yoshida, A. *Parasitol. Int.*, 90: 102617, 2022. doi: 10.1016/j.parint.2022.102617.

- 2) First record of chewing louce *Turdinirmoides vasjukovae* (Mey, 2016) (Ischnocera: Philopteridae) on a long-tailed rosefinch, *Uragus sibiricus* (Pallas, 1773) in Kushiro, Hokkaido, Japan. Yoshino, M. and <u>Asakawa, M.,</u> *Biogeography*, 24; 53-55, 2022. doi.org/10.11358/biogeo.24.95
- 3) Morphology of nematodes belonging to the genus *Rictularia* (Nematoda: Rictulariidae) collected from *Apodemus agrarius* in Shenyang, China. Hasegawa, H. and <u>Asakawa</u>, M.

Jpn. J. Vet. Parasitol., 20: 78-84, 2022.

https://drive.google.com/file/d/17DI5I04eVs3IHjjgzXNjick9dYw3VyMT/view

II. その他<Others>

1) Morphological observation on *Physaloptera species* (Nematoda: Spirurida: Physalopteridae) in murine rodents of Indonesia and East Asian Islands with special reference to their zoogeographical features.

Hasegawa, H., Dewi, K. and Asakawa, M.

Tropic Nat. Hist., 22: 119-129, 2022.

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2) Identification and phylogenetic analysis of *Babesia* parasites in domestic dogs in Nigeria.

Hirata, H., Omobowale, T., Adebayo, O., Asanuma, N., Haraguchi, A., Murakami, Y., Kusakisako, K., Ikeda, K., <u>Asakawa, M.</u>, Suzuki, K., Ishihara, C., Ikadai, H.

- J. Vet. Med. Sci., 84: 338-341, 2022. doi.org/10.1292/jvms.21-0636
- 3) *Cryptosporidium* sp. Mrb001 detected from *Myodes rufocanus bedfordiae*, an indigenous vole of Hokkaido, Japan. Muramatsu, Y., Uchida, L., Tamura, Y. and **Asakawa**, M.
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Tongue worm (subclass: Pentastomida) infection and treatment in two domesticated reptiles – A case report

Youki Takaki ^{a, b, 1}, Takao Irie ^{b, c, 1}, Yoshinori Takami ^a, Mistuhiko Asakawa ^d A M, Ayako Yoshida ^{b, c} A M Show more V

https://doi.org/10.1016/j.parint.2022.102617

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Abstract

Tongue worms (Subclass: Pentastomida) are endoparasites found in carnivorous reptiles, fish, amphibians, birds, and mammals. Several pentastomids cause pentastomiasis, a zoonotic disease. We encountered tongue worm infection in two reptiles imported into Japan: a Wahlberg's velvet gecko (Homopholis wahlbergii) bred in Germany and a wild-caught green tree python (Morelia viridis) from the Republic of Indonesia. The infecting tongue worms were identified as Raillietiella sp. and Armillifer sp. in the gecko and python, respectively, based on morphological and molecular analyses. Gecko is a newly recorded definitive host harboring Raillietiella tongue worm. Live tongue worms were first detected in domestic reptiles in Japan, and this indicates a risk that these tongue worms could be spread to other animals, as well as humans. Therefore, the diagnosis and treatment of infected pets are of importance. In the case of the two infected reptiles, the availability of fecal egg examination for diagnosis was shown. In addition, the effectiveness of treatment with $200~\mu g/kg/day$ ivermectin orally once weekly was demonstrated, without no side-effects and no re-detection of eggs after the cessation of treatment.

出典 doi: 10.1016/j.parint.2022.102617.

最終責任者 Ayako Yoshida and Mitsuhiko Asakawa (Corresponding Authors)

First record of the chewing louse *Turdinirmoides vasjukovae* (Mey, 2016) (Ischnocera: Philopteridae) from Japan

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Abstract: Three adult chewing lice were obtained during post-mortem examination of an adult male Long-tailed Rosefinch, Uragus sibiricus, collected in 2018 at Akan International Crane Center, Kushiro, Hokkaido, Japan. Morphological measurements and characteristics were used to identify the specimens as Turdinirmoides vasjukovae (Mey, 2016), which are the first of this species to be recorded from Japan.

showed that the bird was not infected with Avian Influenza. The rosefinch's measurements were recorded as follows: body

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were elongated, were filiform, had five sections, and reached the corner roots. In addition, the head was not elongated and was 1.05-1.10 times longer than wide; there were mandibulate mouthparts on the ventral part of the head, and the anterior

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出典 doi.org/10.11358/biogeo.24.95

最終責任者 Mitsuhiko Asakawa (Corresponding Author)

Morphology of nematodes belonging to the genus Rictularia (Nematoda: Rictulariidae) collected from Apodemus agrarius in Shenyang, China

Hideo HASEGAWA1) and Mitsuhiko ASAKAWA2)*

ABSTRACT. The morphology of the rictulariid nematode species collected from *Apodemus agrarius* in Shenyang, China, and recorded as *Rictularia cristata* Froelich, 1802, was investigated. Five large gravid females, more than 40 mm long, eight small (circa 2 mm long) immature females shortly after final molt, and two males, were studied. The males showed prominent dimorphism: one had the typical male form with a ventrally-curved tail and developed precloacal fan-like crests; the other resembled a small female in its external morphology and lacked precloacal crests. Identity of the *Rictularia* species parasitic in *Apodemus* spp. of the Far East with *R. cristata* in Europe should be examined using DNA sequence analysis.

KEY WORDS: Rictularia, Apodemus, Shenyang, China, Far East

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出典 https://drive.google.com/file/d/17DI5I04eVs3IHjjgzXNjick9dYw3VyMT/view 最終責任者 Mitsuhiko Asakawa (Corresponding Author)

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Morphological Observation on *Physaloptera* Species (Nematoda: Spirurida: Physalopteridae) in Murine Rodents of Indonesia and East Asian Islands with Special Reference to Their Zoogeographical Features

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Received: 9 September 2021; Accepted: 27 October 2022

ABSTRACT. – Morphological observations of specimens from the genus *Physaloptera* spp. (Spirurida: Physalopteridae) collected from murine species in Indonesia and some islands of East Asia were made. The physalopterid worms found from *Maxomys whiteheadi* and *Maxomys bartelsii* of Kalimantan and West Java, Indonesia, respectively, *Apodemus speciosus* of the Izu Islands, Japan, *Apodemus agrarius* of Jeju Island, Korea, and *Rattus tanezumi* of Uotsuri Island, in the Senkaku Islands, Japan, were identified as *P. apodemi* Wang & Zhang, 2020, previously only reported from Tianjin, China. On the other hand, those in *Rattus argentiventer* of West Java were identified with *P. ngoci* Le-Van-Hoa, 1961 as the first geographical record outside of the continental portion of Southeast Asia. Supplemental morphological remarks were made for *P. apodemi* with special attention to the differentiation from other congeners. The distribution of *P. apodemi* on these small remote islands suggests that dispersal occurred accidentally via synanthropic rats and/or intermediate host insects that possibly escaped from shipwrecks onto these islands.

KEYWORDS: Physaloptera, Maxomys, Apodemus, Rattus, insular distribution, morphology, dispersal

出典 https://lio1.tci-thaijo.org/index.php/tnh/article/view/257331 最終責任者 Hideo Hasegawa (Corresponding Author)

Identification and phylogenetic analysis of Babesia parasites in domestic dogs in Nigeria

Haruyuki Hirata ¹, Temidayo Omobowale ², Olufunke Adebayo ³, Nodoka Asanuma ¹, Asako Haraguchi ⁴, Yoshiki Murakami ¹, Kodai Kusakisako ⁴, Keiko Ikeda ¹, Mitsuhiko Asakawa ¹, Kazuyuki Suzuki ¹, Chiaki Ishihara ¹, Hiromi Ikadai ⁴

Affiliations + expand

PMID: 35110460 PMCID: PMC8983282 DOI: 10.1292/jvms.21-0636

Free PMC article

Abstract

The present study examined the presence of Babesia parasites in 104 domestic dogs in Nigeria. Sequentially, Babesia parasites infecting domestic dogs underwent genetic and phylogenetic analyses. The results of nested PCR based on the Piroplasmida 18S rRNA gene illustrated that 13.5% (14/104) of the samples were positive. The obtained positive samples determined the nucleotide sequences of the 18S rRNA genes. In the genetic and phylogenetic analyses, four of five nucleotide sequences were similar to Babesia canis rossi, and one sample exhibited a close similarity to a Babesia sp. isolated from a raccoon in Hokkaido, Japan. The present study revealed the widespread presence of B. canis rossi among domestic dogs in Nigeria.

Keywords: 18S rRNA; Babesia canis; Nigeria; domestic dog; phylogenetic analysis.

出典 doi.org/10.1292/jvms.21-0636

最終責任者 Hiromi Ikadai (Corresponding Author)

Cryptosporidium sp. Mrb001 detected from Myodes rufocanus bedfordiae, an indigenous vole of Hokkaido, Japan

Yasukazu Muramatsu^{1*}, Leo Uchida¹, Yutaka Tamura² and Mitsuhiko Asakawa³

北海道土着のエゾヤチネズミから分離されたクリプトスポリジウム種、Mrb001株
 村 松 康 和^{1*}・内 田 玲 麻¹・田 村 豊²・浅 川 満 彦³ (Accepted 6 December 2021)

ABSTRACT

Cryptosporidium oocysts were detected from five of 111 grey red-backed voles (Myodes rufocanus bedfordiae) in a forestry area of Hokkaido, which is the northernmost island of Japan and is zoogeographically distinct from the mainland. The number of oocysts per gram of faeces from each vole ranged from 1.5×10^6 to 1.8×10^8 . A partial sequence of small subunit 18S rDNA (SSU rDNA) obtained in this study was registered as Cryptosporidium sp. Mrb001 (GenBank accession no. AB477098) and had the highest similarity to Cryptosporidium sp. 05. 1513.Rb (GenBank accession no. HM015880.1), which originated from drinking water in the United Kingdom (98.5%). Phylogenetic tree analysis indicated that Cryptosporidium sp. Mrb001 clustered with several waterborne Cryptosporidium isolates and other Cryptosporidium spp. that originated from voles that inhabit wetlands in Hokkaido. We provided information about this cryptosporidial parasite isolated from Myodes vole. (139 words) KEYWORDS: Cryptosporidial parasite, small ro-

KEYWORDS: Cryptosporidial parasite, small rodent, wetland, small subunit 18S rDNA

Cryptosporidium are infectious protozoan parasites in the gastrointestinal epithelium of humans and a variety of animals, and they can cause either no symptoms or mild to severe diarrhoea (Horčičková et al. 2018). Some species of cryptosporidial parasites can cause waterborne outbreaks of cryptosporidiosis in industrialised countries (Efstratiou et al. 2017). Host specificity is recognized in cryptosporidial parasites, and voles are reported to be natural hosts and/or reservoirs for at least 20 Cryptosporidium spp. and genotypes (Horčičková et al. 2018). Additionally, the vegetation type of areas inhabited by voles influences Cryptosporidium prevalence (Torres et al. 2000). The grey redbacked vole. Mvodes (formerly Clethrionomys) rufocanus bedfordiae, is a subspecies of M. rufocanus found on Hokkaido and adjacent islands of Japan, and the southern Kurile Islands (Kaneko 1998). In this paper, we provided information on a Cryptosporidium sp. detected from indigenous voles captured from a natural forestry area in Hokkaido, which is the northernmost main island of Japan and is differentiated from mainland Japan by a zoogeographical border called Blakiston's line (McKay

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出典 https://jglobal.jst.go.jp/en/detail?JGLOBAL_ID=201701010943326130 最終責任者 Yasukazu Muramatsu (Corresponding Author)

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- I. 筆頭または責任著者 <First or Corresponding Author>
- Relationship between Escherichia coli virulence factors, notably kpsMTII, and symptoms of clinical metritis and endometritis in dairy cows.
 Yamamura F, Sugiura T, Munby M, Shiokura Y, Murata R, Nakamura T, Fujiki J, <u>Iwano H.</u>

J Vet Med Sci. 2022 Mar 15;84(3):420-428. doi: 10.1292/jvms.21-0586.

2) Biological properties of Staphylococcus virus ΦSA012 for phage therapy. Fujiki J, Nakamura T, Nakamura K, Nishida K, Amano Y, Watanabe Y, Gondaira S, Usui M, Shimizu M, Miyanaga K, Watanabe S, Iwasaki T, Kiga K, Hanawa T, Higuchi H, Sawa T, Tanji Y, Tamura Y, Cui L, <u>Iwano H.</u> *Sci Rep.* 2022 Dec 9;12(1):21297. doi: 10.1038/s41598-022-25352-6.

II. その他<Others>

1) Whole-Genome Sequencing of Pasteurella multocida Strain Pm1, Isolated from a Calf. Gondaira S, Fujiki J, Hirano Y, Murata R, Uchida I, Usui M, Iwasaki T, Okabayashi T, **Iwano H,** Higuchi H.

Microbiol Resour Announc. 2022 Apr 21;11(4):e0004222. doi: 10.1128/mra.00042-22.

2) Bisphenol A-sulfate conjugate disrupts AURKA transcription and cell cycle in BeWo cytotrophoblasts.

Fujiki J, Uchida M, Tsunoda S, Maeda N, Inoue H, Yokota H, <u>Iwano H.</u> *Mol Cell Endocrinol.* 2022 Apr 5;545:111561. doi: 10.1016/j.mce.2022.111561.

scientific reports



OPEN Biological properties of *Staphylococcus* virus ΦSA012 for phage therapy

Jumpei Fujiki¹, Tomohiro Nakamura^{1,2,3}, Keisuke Nakamura¹, Keita Nishida¹, Yurika Amano¹, Yusaku Watanabe¹, Satoshi Gondaira⁴, Masaru Usui⁵, Masaru Shimizu⁶, Kazuhiko Miyanaga⁷, Shinya Watanabe⁷, Tomohito Iwasaki⁸, Kotaro Kiga^{3,7}, Tomoko Hanawa⁸, Hidetoshi Higuchi⁴, Teiji Sawa⁶, Yasunori Tanji², Yutaka Tamura⁵, Longzhu Cui⁷ & Hidetomo Iwano^{1,55}

Staphylococcus virus ФSA012 has a wide host range and efficient lytic activity. Here, we assessed the biological stability of ФSA012 against temperature, freeze-thawing, and pH to clinically apply the phage. In addition, inoculation of ФSA012 through i.p. and i.v. injections into mice revealed that phages were reached the limit of detection in serum and accumulated notably spleens without inflammation at 48 h post-inoculation. Furthermore, inoculation of ФSA012 through s.c. injections in mice significantly induced IgG, which possesses neutralizing activity against ФSA012 and other Staphylococcus viruses, ФSA039 and ФМR003, but not Pseudomonas viruses ФS12-3 and ФR18 or Escherichia viruses T1, T4, and T7 in vitro. Immunoelectron microscopic analysis showed that purified anti-phage IgG recognizes the long-tail fiber of staphylococcus viruses. Although S. aureus inoculation resulted in a 25% survival rate in a mouse i.p. model, ФSA012 inoculation (i.p.) improved the survival rate to 75%; however, the survival rate of ФSA012-immunized mice decreased to less than non-immunized mice with phage i.v. injection at a MOI of 100. These results indicated that ФSA012 possesses promise for use against staphylococcal infections but we should carefully address the appropriate dose and periods of phage administration. Our findings facilitate understandings of staphylococcus viruses for phage therapy.

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最終責任者 Hidetomo Iwano (Corresponding Author)



FULL PAPER

Theriogenology

Relationship between *Escherichia coli* virulence factors, notably *kpsMTII*, and symptoms of clinical metritis and endometritis in dairy cows

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ABSTRACT. Although Escherichia coli is a commensal bacterium of the bovine vaginal microbiota, it is an important pathogenic bacterium that causes diseases of the reproductive tract and subfertility. Recent studies have focused on virulence factors (VFs) of intrauterine E. coll; however, actual endometrial VFs have not been clearly identified. The purpose of this study was to identify the VFs of E. coli associated with clinical metritis and endometritis. Thirty-two strains of E. coli and four mixed Trueperella pyogenes (TP) strains were detected in the uterus of 19 Hoistein dairy cows with obvious clinical signs (between 8 and 66 days postpartum). The presence of six E. coli VFs (fimH, fyuA, kpsMTII, hra1, csgA, and astA) was examined by PCR, and clinical signs and reproductive performance (mixed TP, the percentage of polymorphonuclear neutrophils [PMN%], days to uterine involution, etc.) were evaluated. Four VFs (fimH, hra1, csgA, and astA) were detected in all E. coli strains, whereas fyuA and kpsM7II were detected in 94% and 50% of strains respectively. Cows with E. coll strains harboring kpsMTII exhibited significantly severe clinical scores (vaginal discharge score, PMN%, uterine involution), suggesting that kpsM7li is a key VF for progression of clinical metritis and endometritis. In the present study, we clearly identified six VFs associated with clinical metritis and endometritis. In addition, E. coli strains with kosMTII probably play a crucial role in the progression of clinical metritis and endometritis.

KEY WORDS: Escherichia coli, kpsMTil, postpartum uterine disease, uterine restoration time, virulence factor

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Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

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ABSTRACT Bovine pneumonia is a disease that causes significant economic losses in livestock industries and is vital for animal welfare. The whole-genome sequence of *Pasteurella multocida* strain Pm1, isolated from a calf suffering from pneumonia in Japan, is reported here.

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最終責任者 Hidetoshi Higuchi (Corresponding Author)

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Bisphenol A-sulfate conjugate disrupts AURKA transcription and cell cycle in BeWo cytotrophoblasts



Jumpei Fujiki ^{a, a, a}, Megumi Uchida ^{a, a}, Sakurako Tsunoda ^a, Naoyuki Maeda ^b, Hiroki Inoue ^a, Hiroshi Yokota ^a, Hidetomo Iwano ^a

ARTICLE INFO

Keywords: Placenta Bisphenol BPA EPA Endocrine-disrupting chemicals (EDCs) Solitate-sulfacase pathway

ABSTRACT

Bisphenol A (BPA) has been shown to exhibit various toxic effects, including the induction of reproductive disorders. Generally, BPA is converted to conjugated metabolites, leading to bio-inactivation. On the other hand, the toxicity of conjugated metabolites is not fully understood. Notably, the placenta develops the sulfate-sulfatase pathway, which transports and reactivates sulfated steroids. Therefore, we investigated the potential adverse effects of the BPA-sulfate conjugate (BPA-S) on human placenta-derived BeWo cytotrophoblasts. In the present study, high-concentration BPA-S (100 $\mu\text{M})$ induced significant inhibition of BeWo growth, with effects similar to those seen with unconjugated BPA (100 µM and 100 nM). This growth inhibition was restored by treatment of the cells with an inhibitor of the organic anion-transporting peptides (OATPs) (bromosulphophthalein) or with a sulfatase (STS) inhibitor (STX64). BeWo exhibits expression of the genes encoding OATP1A2 and OATP4A1 as known sulfated steroid transporters and STS, suggesting that BPA-S suppresses cell growth activity via the sulfate-sulfatase pathway. In addition, cell cycle analysis revealed that BPA-S (100 µM) increased the fraction of cytotrophoblasts in the G2/M phases and significantly decreased the accumulation of the transcript encoding Aurora kinase A (AURKA), which is a critical regulator of cellular division. These results suggested that BPA-S triggers cell cycle arrest and inhibits proliferation of BeWo cytotrophoblasts by decreased AURKA, an effect that is mediated by the sulfate-sulfatase pathway. Overall, these findings provide insights into the reactivation of sulfated endocrine-disrupting chemicals and subsequent adverse effects.

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- I. 筆頭または責任著者 <First or Corresponding Author>
- II. その他<Others>
 - Conventional Gel Electrophoresis-Resolvable Insertion/Deletion Markers for Individual Identification, Analysis of Population Genetics in Red-Crowned Cranes in Eastern Hokkaido, Japan

Kawasaki E, Wenjing D., Sawada A., Nakajima M., Momose K., Yoshino T., Amano T., **Endoh D**., Nakajima N., Teraoka H.

Animals 12: 2293. 2022. doi: 10.3390/ani12172293.

- 2) Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler, Contrast-Enhanced Ultrasonography
 - Hanazono K., Itami T., Hayasaka I., Miyoshi K., Hori A., Kato K., **Endoh D**. *Animals* 12: 1175. 2022. doi: 10.3390/ani12091175.
- 3) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

Hanazono K., Nakamoto M., Hori A., Miyoshi K., Nakade T., Itami T., Sano T., Kato K., Ito A., Tanaka K., Yamashita K., **Endoh D.**

Journal of Veterinary Medical Science 84: 1556-1562. 2022. doi: 10.1292/jvms.22-0122





Article

Conventional Gel Electrophoresis-Resolvable Insertion/Deletion Markers for Individual Identification and Analysis of Population Genetics in Red-Crowned Cranes in Eastern Hokkaido, Japan

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Simple Summary: The red-crowned crane is an endangered bird species in the Far East Eurasian continent and Hokkaido, Japan. Individual identification has been achieved with banding and installed transmitters in only a few cranes, though individual identification is essential for various assessments of cranes on their behavioral characteristics, for example. An insertion/deletion (InDel) mutation is a mutation ranging from 1 to 50 bp and is very useful for genetic studies. If primer sets across InDels (>20 bp) can be designed, an InDel polymorphism can be determined with conventional agarose gel electrophoresis, as reported in some plant species. We found a sufficient number of InDel primer sets to be used for individual identification and analysis of population genetics of red-crowned cranes in Hokkaido. The method has additional advantages, such as convenience and low cost, without sequencing and an expensive apparatus.



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Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

by இ Kiwamu Hanazono * ≅ ®, இ Takaharu Itami * ≅ ®, இ Ikuto Hayasaka ≅, இ Kenjiro Miyoshi ≅ ®, இ Ai Hori ≅, இ Keiko Kato ≅ and இ Daiji Endoh ≅ ®

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Simple Summary

Since there is a lack of information regarding how epoprostenol, a prostacyclin, affects canine renal blood flow (RBF), we investigated the effects of short-term administration of epoprostenol at human doses of 2, 5, and 10 ng/kg/min intravenously for 20 min on RBF in six healthy dogs under anesthesia. The effects of short-term administration were investigated. As the dose of epoprostenol increased, peak systolic and end diastolic velocities of the renal arteries, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase. However, these increases were not significant. These results indicate that the administration of human doses of epoprostenol to dogs does not produce significant changes in renal or systemic circulation.

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最終責任者 Kiwamu Hanazono (First and Corresponding Author)



FULL PARIS

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

Kiwamu HANAZONO^{1)*}, Mako NAKAMOTO¹⁾, Ai HORI¹⁾, Kenjiro MIYOSHI¹⁾, Tetsuya NAKADE¹⁾, Takaharu ITAMI¹⁾, Tadashi SANO¹⁾, Keiko KATO¹⁾, Akifumi ITO¹⁾, Kakeru TANAKA¹⁾, Kazuto YAMASHITA¹⁾, Daiji ENDOH¹⁾

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC₅/Ao) and the ratio of long to short diameter of the CVC (CVC₁/CVC₅) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₅/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₅/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC₅/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/CVC₅ of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₅/Ao of the thorax, CVC₁/CVC₅ of the thorax, CVC₅/Ao of the abdomen, and CVC₁/CVC₅ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Effects of digestive drug containing betaine hydrochloride on dry matter intake, rumen profiles, and blood concentrations of gut hormones in non-lactating cows.

Fukumori R, Takayama Y, Izumi K, <u>Oikawa S</u>. *Jpn. J. Anim. Hyg.*, 47, 197-204, 2022

II. その他<Others>

 Sodium butyrate administration modulates the ruminal villus height, inflammationrelated gene expression, and plasma hormones concentration in dry cows fed a highfiber diet.

Fukumori R, Doi K, Mochizuki T, <u>Oikawa S</u>, Gondaira S, Iwasaki T, Izumi K. *Animal Science Journal*, DOI:10.1111/asj.13791, 2022

Effects of digestive drug containing betaine hydrochloride on dry matter intake, rumen profiles, and blood concentrations of gut hormones in non-lactating cows

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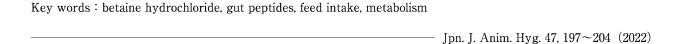
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Summary

The objective of this study was to investigate the effects of digestive drug containing betaine hydrochloride (BH) administration on dry matter intake, the rumen and blood properties in cattle. Four non-lactating cows, each fitted with a rumen cannula, were randomly assigned to 2 treatments in a crossover design. The 2 experimental periods were each 7-d long, with a 3-d washout period separating them. The treatments were oral administration of BH or water (WT). Oral administration was conducted once a day just before feeding. BH was provided as Bio-Pair (TOA Biopharma, CO. Ltd., Tokyo, Japan) at the dose of 90 g/d/cow. Ruminal fluid and blood samples were collected on d 7 over time relative to feeding for determining plasma concentrations of gut hormones (insulin, glucagon like peptide-2 [GLP-2], and ghrelin) and metabolites (glucose, urea-nitrogen, and total-cholesterol) and ruminal concentrations of volatile fatty acids. Dry matter intake was determined from d 5 to 7 of each period for each cow. Ruminal pH was recorded every 15 min through the sample collection period. The pH was not affected by BH administration, but the ruminal propionate proportion was lower and the acetate proportion tended to be higher for cows in the BH group than for cows in the WT group. BH administration decreased the plasma concentrations of glucose and total cholesterol, and increased those of insulin and GLP-2. Regarding ghrelin, an orexigenic hormone, no effect of BH administration was observed, and dry matter intake was not different between the treatments. The above findings indicated that BH did not affect feed intake, but it might affect rumen VFA and blood properties, causing metabolic shifts to anabolism at this dosage of BH.



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最終責任者 Shin Oikawa (Corresponding Author)



Sodium butyrate administration modulates the ruminal villus height, inflammation-related gene expression, and plasma hormones concentration in dry cows fed a high-fiber diet

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Funding information
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Abstract

The objectives of this study were to evaluate the effects of sodium butyrate on the ruminal villus morphology, mRNA expression associated with nutrient metabolism and inflammation in the ruminal epithelium, and plasma concentrations of metabolites and hormones in non-lactating cows fed a high-fiber diet. Four Holstein cows with a rumen cannula were assigned to two treatments in a crossover design. The treatments were ruminal administration of sodium butyrate premix or control premix before feeding to cows fed the same total mixed ration mainly composed of glass silage once a day. Sodium butyrate was provided at a butyrate dose of 0.04% per kg body weight. The control premix was made by replacing sodium-butyrate with wheat bran. The plasma β-hydroxybutyrate concentration increased 3 to 6 h after the butyrate premix administration but returned to a concentration similar to that of the control before feeding. After continuous administration, increases in the ruminal villus height and plasma concentration of glucagon-like peptide-2, and lower gene expression of TNF-α, IL-1 β, and TLR-2 in the rumen epithelium were observed in cows supplied with the butyrate premix. These results showed that sodium butyrate affects rumen epithelial morphology and plasma concentrations of hormones even under a low fermentable diet.

KEYW ORDS

butyrate, dairy cow, GLP-2, inflammation-related gene, rumen papillae

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生產動物病態学(Farm Animal Pathophysiology)

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Mori K, Otomaru K, Kato T, Yokota O, <u>Ohtsuka H</u>. Field Trial of Antibody Response to Inactivated Bacterial Vaccine in Young Holstein Calves: Influence of Animal Health Status. *J Vet Res.* 25,109-116. 2022. doi: 10.2478/jvetres-2022-0003.
- II. その他<Others>



Field trial of antibody response to inactivated bacterial vaccine in young Holstein calves: influence of animal health status

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Abstract

Introduction: Bovine respiratory disease (BRD) is one of the primary causes of death in young calves. Vaccination against infection by the common bacteria causing BRD is possible; however, the physical condition of the young calves that enables antibody production when stimulated by early immunisation remains to be elucidated. Material and Methods: Healthy young female Holstein calves on a commercial dairy farm were fed a colostrum replacer and administered primary and booster immunisations with an inactivated vaccine against the bacterial pneumonia agents Histophilus somni, Pasteurella multocida and Mannheimia haemolytica. At each immunisation, the body weight and height at the withers were measured and the body mass index (BMI) was calculated. Blood was sampled immediately before immunisation and 3 weeks following the booster. The calves were divided into positive and negative groups based on the antibody titre at the final blood sampling. Maternal antibody titres at the primary immunisation and BMI, nutritional status and oxidative stress at both immunisations were compared between the two groups. Results: Antibody titre at the primary and BMI at both immunisations were significantly higher in the positive than in the negative group (P < 0.05). Additionally, serum gamma globulin was significantly higher in the positive group (P < 0.05), indicating a strong correlation between maternal antibody and serum gamma globulin levels. Conclusion: Elevated maternal antibody titre and higher BMI are positive factors for successful early immunisation, for which suitable colostrum may also be fundamental in young calves administered inactivated vaccines.

Keywords: early vaccination, bovine respiratory disease, maternal antibody, nutritional status, oxidative stress.

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep.

Onaga T, Yasui Y, Hayashi H

General and Comparative Endocrinology 326:114073, 2022.

doi: https://doi.org/10.1016/j.ygcen.2022.114073

2) Intravenous administration of xenin-25 accelerates cyclic ruminal contractions in healthy conscious sheep.

Onaga T, Sakai A., Yasui Y.

Neuropeptides 96:102293, 2022.

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II. その他<Others>



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Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep

Takenori Onaga ***, Yumiko Yasui *, Hideaki Hayashi b

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Keywords Ranyma Bicselsonate Cholinergic nerve Nontrotesiain receptor Asstagoniss

ABSTRACT

The present study aimed to clarify the effects of neurotensin and xenin on pancreatic exocrine secretion in conscious sheep and their mechanism of actions. The animals were equipped with two sliastic cannulae in the common bile duct to separately collect pancreatic fluid and bile, and a silastic cannula in the proximal duodenum to continuously return the mixed fluids. NT and xenin were intravenously injected at range of 0.01,-3.0 nmol/kg during the phase I of duodenal migrating motor complex. A single intravenous NT injection significantly and dose-dependently increased pancreatic fluid, protein, and bicarbonate outputs. The effect of NT at 1 nmol/kg was completely inhibited by a background intravenous infusion of atropine methyl nitrate at a dose of 10 nmol/kg/ min, however, the effect was not altered by a prior injection of the neurotensin receptor subtype (NTE)-1 antagonist SR 48692 at 60 nmol/kg. Moreover, a single intravenous xenin-25 injection significantly and dosedependently increased pancreatic fluid and protein output, whereas the effect of xenin-25 did not clearly show dose-dependence. The prior 58 49692 injection at 30 nmol/kg did not significantly alter the effects of xenin-25 at 0.3 nmol/kg, while the stropine infusion significantly inhibited the increase in fluid secretion. Under the atropine infusion, xenin-25 at 0.3 nmol/kg did not increase protein and bicarbonate outputs, whereas the inhibitory effect of the stropine was not significant compared to that of the single injection of xenin-25. A single intravenous injection of NTR-2 agonist levocabastine at 0.1-3 nmol/kg did not alter pancreatic exocrine secretion. These results suggest that both NT and xenin-25 effectively stimulates pancreatic exocrine secretion through the peripheral cholinergic system in sheep and that MTS-2 is not involved in the regulation of pancreatic exocrine secretion, however, we did not precisely determine the role of NTR-1 in the actions of both the poptides on pancreatic exocrine secretion.

1. Introduction

Xenin and neurotensin (NT) are abundantly localized in the mucosa in the upper and lower gastrointestinal (GI) tract in mammals, respecm. 1976: Fe et al., 1977). Despite a difference in the peptides distribution in the GI tract, they have similar conserved amino acid sequences at the caroboxyl (C)-terminal of the molecules. NT acts on three major subtypes of neurotensia receptors (NTR), i.e., NTR type-1 (NTR-1), NTR type-2 (NTR-2), and NTR type-3 (NTR-3) (Visitent et al., 1999). NTR-1 and -2 are localized in the cell membrane of the target cells, that transfer the extracellular peptide signals to the intracellular messenger system,

while NTR-3, a sortilin receptor, is localized in the intracellular organelle and does not belong to G-protein coupled receptor superfamily (Mazella et al., 1998). Due to the high homology between the C-terminal amino acid sequence of the peptides, xenin has an affinity to NTR-1 (Feurle et al., 1996). Limiting to the four amino acids at the C-terminus, mammalian neuromedin N and chicken LANT-6 also have high homology with NF and xenin (Carraway et al., 1993; Ferris, 1989). However, why these peptides have similar binding activity to the NTR superfamily in the process of animal evolution remains unknown.

Xenopsin, an amphibian skin octapeptide, is the ancestor molecule of xenin (Feorle et al., 1992), while the amino acid sequence of xenin has high homology with N-terminal sequence of the costomer protein

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Abbreviations: NT, Neurotensin; NTR, Neurotensin receptor.

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Neuropeptides







Intravenous administration of xenin-25 accelerates cyclic ruminal contractions in healthy conscious sheep

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ARTICLE INFO

Keywoods Sheep Forestonach Bunen contractions Xearosia, related peptides

ABSTRACT

The present study aimed to determine the effect and mode of action of the intravenous injection of xenin-25 on cyclic contractions of the rumen in healthy conscious sheep and mode of its action. Clinically healthy male sheep were equipped with a rumen cannuls by surgery under anesthesia, and numinal contractions were recorded with manometry in conscious animals after the recovery period. Intravenous xenin-25 injection induced a cluster of premature ruminal phasic contractions in a dose-dependent manner between 0.03 and 1 mmol/kg, and the change at the highest dose was statistically significant. In contrast, intravenous neurotensin injection inhibited the amplitude of cyclic numen contractions. The xenin-25 effect was not significantly altered by prior injection of the neurotensin receptor subtype-1 antagonist SR 48892 at 30 and 100 nmol/kg. After exhanasis the ruminal muscles were excised for its view experiments. A single xenin-25 application (0.3-10 µM) to the longitudinal and circular muscle strips of the rumen did not induce any change in tension or electric field stimulation-induced phasic contractions of the muscle strips. These results demonstrated that circulating xenin-25 stimulates rumen contractions by acting on sites except the intramural intrinsic nerve piexus or smooth muscles of the rumen, implying that xenin-25 acts on the gastric center and/or cholinergic efferent nerve innervated to the ovine rumen.

1. Introduction

Xenin is a homologous peptide with xenopsin, an ancestoral octapeptide in amphibians (Feorle et al., 1992; Sures and Crippa, 1984). In humans, xenin consists of 25 amino acids, and 6 amino acid sequences of xenin-25 at the carboxyl terminus are identical to that of xenopsin. The common sequence of the peptides is also identical to the carboxyl terminal 4 amino acid sequence of neurotensin (NT), although they skip over one residue. Therefore, xenin and NT have been shown to act on the same family of peptide receptors as NT receptor type-1 (NTR-1) (Feurle, 1998; Feurle et al., 1992).

Xenopsin is distributed in the skin of amphibian, while xenin is distributed in the gastric mucosa of canines and humans (Carraway and Mitra, 1990; Rix et al., 1986). This distribution of xenin differs from that of NT, which is distributed in the distal intestine, particularly the ileum, in many mammalian species (Notice et al., 1982; Sundler et al., 1977). Variety effects of xenin-25 on mammalian gastrointestinal (GI) tract endocrine tissue has been clarified over the last two decades (Chowdhury et al., 2013; Gault et al., 2015; Kaji et al., 2017; Kim and Mizuno,

2016; Kuwahara et al., 2019; Wice et al., 2012; Wice et al., 2010). In ruminant species, we demonstrated major localization of endocrine cells of xenin in the ovine abomasum and duodenum in the GI tract (Onaga et al., 2020). The amino acid sequences of ovine xenin-25 were confirmed to be identical to those of humans, rats, and mice. We then clarified that intravenous (i.v.) xenin-25 injection increases basal insulin secretion but not glucagon, in conscious sheep, and augments glucose-induced insulin secretion, indicating that xenin plays a crucial role in glucose metabolism in sheep (Onaga et al., 2021).

Ruminant species have a characteristic forestomach with a huge rumen serving as a fermentation chamber, and the digestion rate and retention time of feed in ruminal fermentation influence nutrients and energy metabolism in ruminants (Hofmann, 1989). Periodic rumen contractions regulate the mixing rate of digesta in the rumen and its outflow to the lower GI tract (Ruckebusch, 1989), and accelerate luminal fermentation by microbe that supplies short chain fatty acids as a primary energy source to ruminants. Therefore, activity and regulation of cyclic rumen contractions plays a crucial role in controlling not only digestion but also appetite and nutrition in animals (Groyvan, 1979;

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- I. 筆頭または責任著者 <First or Corresponding Author>
- Ubiquitin-specific protease 2 in the ventromedial hypothalamus modifies blood glucose levels by controlling sympathetic nervous activation Hashimoto M, Fujimoto M, Konno K, Lee ML, Yamada Y, Yamashita K, Toda C, Tomura M, Watanabe M, Inanami O, <u>Kitamura H.</u>
 - J. Neurosci. 42: 4607-4618, 2022. doi: 10.1523/JNEUROSCI.2504-21.2022
- 2) Application of the colorimetric loop-mediated isothermal amplification (LAMP) technique for genotyping *Cre*-driver mice

Fujimoto M, Kitamura H.

J. Vet. Med. Sci. 84:507-510, 2022. doi: 10.1292/jvms.21-0658

II. その他<Others>

1) Association of lithocholic acid with skeletal muscle hypertrophy through TGR5-IGF-1 and skeletal muscle mass in cultured mouse myotubes, chronic liver disease rats and humans.

Tamai Y, Eguchi A, Shigefuku R, <u>Kitamura H</u>, Tempaku, M, Sugimoto R, Kobayashi Y, Iwasa M, Takei Y, Nakagawa H.

Elife 11: e80638, 2022. doi: 10.7554/eLife.80638

J. Neurosci. 42: 4607-4618, 2022

Cellular/Molecular

Ubiquitin-Specific Protease 2 in the Ventromedial Hypothalamus Modifies Blood Glucose Levels by Controlling Sympathetic Nervous Activation

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Ubiquitin-specific protease 2 (USP2) participates in glucose metabolism in peripheral tissues such as the liver and skeletal muscles. However, the glucoregulatory role of USP2 in the CNS is not well known. In this study, we focus on USP2 in the ventromedial hypothalamus (VMH), which has dominant control over systemic glucose homeostasis. ISH, using a *Usp2*-specific probe, showed that *Usp2* mRNA is present in VMH neurons, as well as other glucoregulatory nudei, in the hypothalamus of male mice. Administration of a USP2-selective inhibitor ML364 (20 ng/head), into the VMH elicited a rapid increase in the circulating glucose level in male mice, suggesting USP2 has a suppressive role on glucose mobilization. ML364 treatment also increased serum norepinephrine concentration, whereas it negligibly affected serum levels of insulin and corticosterone. ML364 perturbated mitochondrial oxidative phosphorylation in neural SH-SY5Y cells and subsequently promoted the phosphorylation of AMP-activated protein kinase (AMPK). Consistent with these findings, hypothalamic ML364 treatment stimulated AMPK α phosphorylation in the VMH. Inhibition of hypothalamic AMPK prevented ML364 from increasing serum norepinephrine and blood glucose. Removal of ROS restored the ML364-evoked mitochondrial dysfunction in SH-SY5Y cells and impeded the ML364-induced hypothalamic AMPK α phosphorylation as well as prevented the elevation of serum norepinephrine and blood glucose levels in male mice. These results indicate hypothalamic USP2 attenuates perturbations in blood glucose levels by modifying the ROS-AMPK-sympathetic nerve axis.

Key words: hypothalamus; mitochondria; reactive oxygen species; ubiquitin-specific protease 2; ventromedial hypothalamus

Significance Statement

Under normal conditions (excluding hyperglycemia or hypoglycemia), blood glucose levels are maintained at a constant level. In this study, we used a mouse model to identify a hypothalamic protease controlling blood glucose levels. Pharmacological inhibition of USP2 in the VMH caused a deviation in blood glucose levels under a nonstressed condition, indicating that USP2 determines the set point of the blood glucose level. Modification of sympathetic nervous activity accounts for the USP2-mediated glucoregulation. Mechanistically, USP2 mitigates the accumulation of ROS in the VMH, resulting in attenuation of the phosphorylation of AMPK. Based on these findings, we uncovered a novel glucoregulatory axis consisting of hypothalamic USP2, ROS, AMPK, and the sympathetic nervous system.

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The Journal of Veterinary Medical Science



NOTE

Laboratory Animal Science

Application of the colorimetric loopmediated isothermal amplification (LAMP) technique for genotyping *Cre*-driver mice

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ABSTRACT. The Cre-loxP system is widely used to investigate the cell-type specific roles of genes of interest. Cre-driver mice are required for cell-type specific knockout during the Cre-loxP reaction. To maintain Cre-driver mouse strains, Polymerase chain reaction (PCR)-oriented genotyping targeting the Cre gene cassette is usually conducted. In this study, we instead applied a colorimetric loop-mediated isothermal amplification (LAMP) method for Cre-genotyping. Among four sets of primers designed by the in silico program, one set effectively amplified the Cre cassette of three Cre-driver strains, but not of C57BL/6 mice. This LAMP-oriented method reduces assay time by less than half compared to the PCR-based method, and can be carried out using a conventional isothermal incubator. Applying this LAMP method may accelerate genotyping of Cre-driver mice.

KEYWORDS: conditional knockout, Cre, genotyping, loop-mediated isothermal amplification

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最終責任者 Hiroshi Kitamura (Corresponding Author)





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Association of lithocholic acid with skeletal muscle hypertrophy through TGR5-IGF-1 and skeletal muscle mass in cultured mouse myotubes, chronic liver disease rats and humans

Yasuyuki Tamai^{1†}, Akiko Eguchi^{1*†}, Ryuta Shigefuku¹, Hiroshi Kitamura², Mina Tempaku¹, Ryosuke Sugimoto¹, Yoshinao Kobayashi³, Motoh Iwasa¹, Yoshiyuki Takei¹, Hayato Nakagawa¹

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Abstract

Background: Hepatic sarcopenia is one of many complications associated with chronic liver disease (CLD) and has a high mortality rate; however, the liver-muscle axis is not fully understood. Therefore, few effective treatments exist for hepatic sarcopenia, the best of which being branched-chain amino acid (BCAA) supplementation to help increase muscle mass. Our aim was to investigate the molecular mechanism(s) of hepatic sarcopenia focused on bile acid (BA) composition.

Methods: The correlation between serum BA levels and psoas muscle mass index (PMI) was examined in 73 CLD patients. Gastrocnemius muscle phenotype and serum BA levels were assessed in CLD rats treated with BCAA. Mouse skeletal muscle cells (C2C12) were incubated with lithocholic acid (LCA), G-protein-coupled receptor 5 (TGR5) agonist or TGR5 antagonist to assess skeletal muscle hypertrophy.

Results: In human CLD, serum LCA levels were the sole factor positively correlated with PMI and were significantly decreased in both the low muscle mass group and the deceased group. Serum LCA levels were also shown to predict patient survival. Gastrocnemius muscle weight significantly increased in CLD rats treated with BCAA via suppression of protein degradation pathways, coupled with a significant increase in serum LCA levels. LCA treated C2C12 hypertrophy occurred in a concentration-dependent manner linked with TGR5-Akt pathways based upon inhibition results via a TGR5 antagonist.

Conclusions: Our results indicate LCA-mediated skeletal muscle hypertrophy via activation of TGR5-IGF1-Akt signaling pathways. In addition, serum LCA levels were associated with skeletal muscle mass in cirrhotic rats, as well as CLD patients, and predicted overall patient survival.

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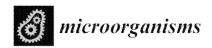
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- I. 筆頭または責任著者 <First or Corresponding Author>
 - 1) **Kirisawa R**, Kato R, Furusaki K, Onodera T. Universal Virucidal Activity of Calcium Bicarbonate Mesoscopic Crystals That Provides an Effective and Biosafe Disinfectant. *Microorganisms*. 10: 262. 2022.

doi: 10.3390/microorganisms10020262.

II. その他<Others>





Article

Universal Virucidal Activity of Calcium Bicarbonate Mesoscopic Crystals That Provides an Effective and Biosafe Disinfectant

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Abstract: We investigated the virucidal effects in solution of a new type of disinfectant, calcium bicarbonate mesoscopic crystals, designated CAC-717, against various types of virus. CAC-717 in solution is alkaline (pH 12.4) and has a self-electromotive force that generates pulsed electrical fields. Upon application to human skin, the pH of the solution becomes 8.4. CAC-717 contains no harmful chemicals and is thus non-irritating and harmless to humans and animals. Its virucidal effects were tested against six types of animal virus: enveloped double-strand (ds)-DNA viruses, non-enveloped ds-DNA viruses, non-enveloped single strand (ss)-DNA viruses, enveloped ss-RNA viruses, non-enveloped ss-RNA viruses, and non-enveloped ds-RNA viruses. The treatment resulted in a reduction in viral titer of at least 3.00 log₁₀ to 6.38 log₁₀. Fetal bovine serum was added as a representative organic substance. When its concentration was ≥20%, the virucidal effect of CAC-717 was reduced. Real-time PCR revealed that CAC-717 did not reduce the quantity of genomic DNA of most of the DNA viruses, but it greatly reduced that of the genomic RNA of most of the RNA viruses. CAC-717 may therefore be a useful biosafe disinfectant for use against a broad range of viruses.

Keywords: calcium bicarbonate; mesoscopic crystals; animal viruses; disinfectant; foot-and-mouth disease virus; SARS-CoV-2; virucidal activity



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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Mastitis causes negative reproduction performance like genital diseases.

Kitade Y., Tsukano K., Miyamoto Y., Suzuki K.

Res Vet Sci. 153: 35-44. 2022. doi: 10.1016/j.rvsc.2022.10.002.

2) Endotoxin activity and leukocytic STAT3 mRNA alterations differ according to age in lipopolysaccharide-challenged calves.

Nishi Y., Murakami Y., Teshima S., Tsukano K., Otsuka M., Hirata H., Tsuchiya M., Suzuki K.

Res Vet Sci. 152: 300-306. 2022. doi: 10.1016/j.rvsc.2022.08.028.

3) Comparison of the alkalizing abilities between 1.35% sodium bicarbonate solutions with and without dextrose in healthy calves.

Sato K., Tsukano K., Kurata M., Ajito T., Hirata H., Suzuki K.

J. Vet. Med. Sci. 84(10): 1335-1339. 2022. doi: 10.1292/jvms.22-0289.

4) Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs.

Murakami Y., Tsukano K., Hirata H., Koie H., Suzuki K.

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Hirata H, Omobowale T, Adebayo O, Asanuma N, Haraguchi A, Murakami Y,

Kusakisako K, Ikeda K, Asakawa M, Suzuki K, Ishihara C, Ikadai H.

J. Vet. Med. Sci. 84(3): 338-341. 2022. doi: 10.1292/jvms.21-0636



Contents lists available at Science Meet

Research in Veterinary Science

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Mastitis causes negative reproduction performance similar to genital diseases

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ARTICLE INFO

Keywords: Mastitis Genital diseases Days open Risk factor

ABRTRACT

The economic efficiency of dairy farms is directly influenced by reproductive performance. Reproductive performance is affected by postpartum health; however, it is unknown which diseases reduce reproductive performance or how often these diseases occur in tie-stall dairy farms. In this study, the 15 most frequent diseases in tie-stalls and their impact on reproduction were determined by logistic analysis. Data from reproductive and veterinary records of 814 cows (473 Holstein) calving between April 2016 and March 2018 reared in 9 tie-stall commercial dairy farms were used. The 15 most frequent diseases were identified by medical records. The odds ratio (OR) of the diseases reducing reproductive performance (days open, number of artificial insemination, and first artificial insemination days in milk) was measured by logistic regression analysis. We focused on mastitis, and factors (inflammation grade, causative bacteria) having a negative effect on reproduction were measured similarly. Of the 15 most frequent diseases, endometritis (OR: 5.45, p < 0.001), ovarian quiescence (OR: 3.95, p = 0.001), ovarian quiescence (OR: 3. < 0.001), mastitis (OR: 2.49, p < 0.001), and follicular cyst (OR: 2.33, p \approx 0.006) significantly prolonged days open after adjusting for environmental factors (farm, parity, and calving season). Focusing on mastitis, mastitis with mild inflammation significantly prolonged days open. Mastitis and genital diseases were frequent diseases that reduced reproductive performance. Strategies to reduce the incidence of these diseases are considered effective for the economics of tie-stall dairy farms.

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Endotoxin activity and leukocytic STAT3 mRNA alterations differ according to age in lipopolysaccharide-challenged calves

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ARTICLE INFO

Keywords: Acute phase response Calf Endotoxin STAT3

ABSTRACT

The objective of this study was to investigate the age difference in the response to endotoxin in calves related to the plasma endotoxin activity and mRNA expression of cytokines. Fifteen calves were divided into three groups: control (191 \pm 21 days), weaning (162.4 \pm 17.5 days), and calf (22.4 \pm 8.2 days). The weaning and calf groups received 2.5 µg/kg of ultrapure O111:B4 LPS in 10 mL of each autologous serum, whereas the control calves received a similar volume of saline. Blood samples were collected at 0, 0.5, 1, 2, 4, 8, 12, and 24 h. Liver samples were collected by ultrasound-guided liver biopsy at 0, 2, 4, and 24 h. Plasma endotoxin activity was measured by the limulus amebocyte lysate kinetic turbidimetric assay. The mRNA expression level of GAPDH, TLR-4, NF-xB2, TNF-α, IL-6, and STAT3 in leukocytes and the liver was measured by real-time PCR.

Following LPS challenge, the maximal plasma endotoxin activity, and leukocytic expression of TLR4, NF-xB2, TNF-a, and STAT3 were reached at 0.5, 4, 2-4, 2-4, and 4 h, respectively, in weaning and calf groups. The endotoxin activity in calf remained high until 2 h. Furthermore, the expression of leukocytic STAT3 mRNA in calf was not significantly different from the pre-value. In contrast, STAT3 mRNA in weaning markedly increased at 2 and 4 h. Therefore, this study provides new information to the literature of immune and inflammatory responses in calves.

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FULL PAPER

Internal Medicine

Comparison of the alkalizing abilities between 1.35% sodium bicarbonate solutions with and without dextrose in healthy calves

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ABSTRACT. The present study aimed to clarify the alkalizing ability of 1.35% isotonic sodium bicarbonate solution (ISBS), which did not contain dextrose, compared with that of 1.35% isotonic bicarbonate sodium solution containing 4.03% dextrose (ISBD) in healthy calves. The calves were intravenously administered with 20.7 mL/kg of the solutions for 30 min as the volume required to correct base deficit of 10 mM. ISBS increased the blood pH, HCO $_3^-$, and base excess from 7.44 \pm 0.02, 29.6 \pm 1.9 mM, and 5.3 \pm 2.1 mM to 7.49 \pm 0.02, 36.9 \pm 2.3 mM, and 13.5 \pm 2.6 mM respectively (P<0.05). These factors for the ISBD group increased from 7.41 \pm 0.02, 29.0 \pm 1.1 mM, and 4.5 \pm 1.3 mM to 7.43 \pm 0.02, 33.5 \pm 1.9 mM, and 9.5 \pm 1.7 mM (P<0.05), respectively. Furthermore, in the ISBD group, the relative plasma volume and blood glucose level increased while the K+ level decreased, which did not occur in the ISBS group. Therefore, the results revealed that ISBS had better alkalizing ability in calves than ISBD.

KEYWORDS: calf, dextrose, hyperkalemia, isotonic sodium bicarbonate, metabolic acidosis

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Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs

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Hiroshi KOIE² Kazuyuki SUZUKI¹*

Abstract

This study aimed to investigate, using magnetic resonance imaging, whether continuous hypertonic saline (HSS) infusion induces a superior vasodilating effect on the encephalic vessels compared to bolus infusion in dogs. The relative cross-sectional area of superior sagittal sinus increased to 1.96 ± 0.09 and 1.69 ± 0.31 times of the pre-value in the continuous and bolus groups, respectively, at t=30 min (p<0.001). However, the relative cross-sectional area of superior sagittal sinus was larger in the continuous group than that in the bolus group (p<0.001). The results suggest that continuous infusion of HSS might be superior to bolus infusion in inducing vasodilatation of the encephalic circulation.

Keywords: encephalic circulation, fluid therapy, hypertonic saline, magnetic resonance imaging, superior sagittal sinus

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NOTE

Parasitology

Identification and phylogenetic analysis of Babesia parasites in domestic dogs in Nigeria

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J. Vet. Med. Sci. 84(3): 338–341, 2022 doi: 10.1292/jvms.21-0636

Received: 28 November 2021 Accepted: 23 January 2022 Advanced Epub: 2 February 2022 ABSTRACT. The present study examined the presence of *Babesia* parasites in 104 domestic dogs in Nigeria. Sequentially, *Babesia* parasites infecting domestic dogs underwent genetic and phylogenetic analyses. The results of nested PCR based on the Piroplasmida 185 rRNA gene illustrated that 13.5% (14/104) of the samples were positive. The obtained positive samples determined the nucleotide sequences of the 185 rRNA genes. In the genetic and phylogenetic analyses, four of five nucleotide sequences were similar to *Babesia canis rossi*, and one sample exhibited a close similarity to a *Babesia* sp. isolated from a raccoon in Hokkaido, Japan. The present study revealed the widespread presence of *B. canis rossi* among domestic dogs in Nigeria.

KEY WORDS: 18S rRNA, Babesia canis, domestic dog, Nigeria, phylogenetic analysis

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Metabarcoding of feces and intestinal contents to determine carnivorous diets in redcrowned cranes in eastern Hokkaido, Japan.

Kataoka H, Koita N, Ito Kondo N, Ito HC, Nakajima M, Momose K, Iima H, Yoshino T, Amano T, Kitazawa T, Endoh D, Nakajima N, <u>Teraoka H.</u> *J Vet Med Sci.* 2022. 84, 358-367. doi: 10.1292/jvms.21-0516.

2) Conventional Gel Electrophoresis-Resolvable Insertion/Deletion Markers for Individual Identification and Analysis of Population Genetics in Red-Crowned Cranes in Eastern Hokkaido, Japan.

Kawasaki E, Wenjing D, Sawada A, Nakajima M, Momose K, Yoshino T, Amano T, Endoh D, Nakajima N, <u>Teraoka H</u>.

Animals (Basel). 2022. 12, 2293. doi: 10.3390/ani12172293

Ⅱ. その他<Others>

1) Cytochrome P450 2J Genes Are Expressed in Dogs, Cats, and Pigs, and Encode Functional Drug-Metabolizing Enzymes.

Uno Y, Murayama N, Ijiri M, Kawaguchi H, Yamato O, Shiraishi M, Asano A, **Teraoka H**, Mizukawa H, Nakayama SMM, Ikenaka Y, Ishizuka M, Yamazaki H. *Drug Metab. Dispos.* 2022. 50, 1434-1441. doi: 10.1124/dmd.122.000930.



FULL PAPER

Wildlife Science

Metabarcoding of feces and intestinal contents to determine carnivorous diets in red-crowned cranes in eastern Hokkaido, Japan

Haruka KATAOKA¹, Nanami KOITA¹, Natsuko ITO KONDO², Hiroshi C. ITO², Momoko NAKAJIMA², Kunikazu MOMOSE³, Hiroko IIMA⁴, Tomoo YOSHINO⁴, Tomoko AMANO⁵, Takio KITAZAWA¹, Daiji ENDOH¹, Nobuyoshi NAKAJIMA²) and Hiroki TERAOKA^{1,3}*

ABSTRACT. The red-crowned crane Grus japonensis in Hokkaido, Japan forms a closed population as a residence that is independent of the mainland population. Based on observations of a limited number of individuals as well as cranes in captivity, red-crowned cranes are omnivores and eat fish, worms, insects and plants in their own territories except in winter, when they are fed with dent corn that is supplied in eastern Hokkaido. DNA metabarcoding based on high throughput sequencing was carried out using universal primer sets for cytochrome oxidase subunit I gene. Feces from 27 chicks collected in June and July in the period from 2016 to 2018 and intestinal contents from 33 adult and subadult cranes that were found dead almost throughout year in 2006-2013 in the field in eastern Hokkaido were used. Although compositions varied considerably in the cranes, both insects and fish were found in adults and subadults to the same extents, while insects were predominant in chicks. Both insects and fish were detected in all seasons for adults and subadults. Horse flies, scarab beetles and weevils accounted for the most of the insects regardless of the life stage. Dace, stickleback, flatfish and sculpin were the major fish species in adults, while chicks ate almost only stickleback. The results provide the first comprehensive data on carnivorous diets in wild red-crowned cranes in eastern Hokkaido as basis for conservation of red-crowned cranes, for which the life style and area continue to change.

KEY WORDS: cytochrome c oxidase subunit I, Grus japonensis, high throughput sequencing, Japan, scatology

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Article

Conventional Gel Electrophoresis-Resolvable Insertion/Deletion Markers for Individual Identification and Analysis of Population Genetics in Red-Crowned Cranes in Eastern Hokkaido, Japan

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Simple Summary: The red-crowned crane is an endangered bird species in the Far East Eurasian continent and Hokkaido, Japan. Individual identification has been achieved with banding and installed transmitters in only a few cranes, though individual identification is essential for various assessments of cranes on their behavioral characteristics, for example. An insertion/deletion (InDel) mutation is a mutation ranging from 1 to 50 bp and is very useful for genetic studies. If primer sets across InDels (>20 bp) can be designed, an InDel polymorphism can be determined with conventional agarose gel electrophoresis, as reported in some plant species. We found a sufficient number of InDel primer sets to be used for individual identification and analysis of population genetics of red-crowned cranes in Hokkaido. The method has additional advantages, such as convenience and low cost, without sequencing and an expensive apparatus.

Abstract Red-crowned crane $Grus\ japonensis$ is an endangered species in two separate populations: the mainland population in the Eurasian continent and the island population in eastern Hokkaido, Japan. We found 11 insertion/deletion (InDel) markers in the genome of the red-crowned crane and designed primer sets across these InDels that can be analyzed with conventional agarose gel electrophoresis. Sixty-six samples of whole blood and skeletal muscle obtained from red-crowned crares, including 12 families in eastern Hokkaido from 1994 to 2021, showed different patterns in gel images of 11 InDel PCR reactions except for two pairs. The combined non-exclusion probability of the 11 markers indicates that individuals can be determined with a probability of 99.9%. In 39 non-relative chicks, the expected heterozygosity (He) was 0.316, suggesting low genetic diversity. This might not be caused by high levels of inbreeding since the average FIS was not significantly different from zero (0.095, p = 0.075). The results suggest that the 11 InDel primer sets can be used for fairly accurate individual identification as well as genetic population analyses in red-crowned cranes in the island population.



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最終責任者 Hiroki Teraoka (Corresponding Author)

Cytochrome *P450 2J* Genes Are Expressed in Dogs, Cats, and Pigs, and Encode Functional Drug-Metabolizing Enzymes

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ABSTRACT

Cytochrome P450s (P450s) have been identified and analyzed in dogs and pigs, species that are often used in preclinical drug studies. Moreover, P450s are clinically important for drug therapy not only in humans, but also in species under veterinary care, including dogs and cats. In the present study, seven P450s homologous to human CYP2J2, namely, dog CYP2J2; cat CYP2J2; and pig CYP2J33, CYP2J35, CYP2J91, and CYP2J93, were newly identified and characterized, along with pig CYP2J34 previously identified. The cDNAs of these CYP2Js contain open reading frames of 502 amino acids, except for CYP2J35 (498 amino acids), and share high sequence identity (77%-80%) with human CYP2J2. Phylogenetic analysis revealed that dog and cat CYP2J2 were closely related, whereas pig CYP2Js formed a cluster. All seven CYP2J genes contain nine coding exons and are located in corresponding genomic regions, with the pig CYP2J genes forming a gene cluster. These CYP2J2 mRNAs were predominantly expressed in the small intestine with additional expression in the kidney and brain for dog CYP2J2 and pig CYP2J91 mRNAs, respectively. All seven CYP2Js metabolized human CYP2J2 substrates terfenadine, ebastine, and astemizole, indicating that they are functional enzymes. Dog CYP2J2 and pig CYP2J34 and CYP2J35 efficiently catalyzed ebastine primary hydroxylation and secondary carebastine formation at low substrate concentrations, just as human CYP2J2 does. Velocity-versus-substate plots exhibited sigmoidal relationships for dog CYP2J2, cat CYP2J2, and pig CYP2J33, indicating allosteric interactions. These results suggest that dog, cat, and pig CYP2Js have similar functional characteristics to human CYP2J2, with slight differences in ebastine and astemizole oxidations.

SIGNIFICANCE STATEMENT

Dog CYP2J2; cat CYP2J2; and pig CYP2J33, CYP2J34, CYP2J35, CYP2J91, and CYP2J93, homologous to human CYP2J2, were identified and characterized by sequence, phylogenetic, and genomic structure analyses. Intestinal expression patterns of CYP2J mRNAs were characteristic in dogs, cats, and pigs. Dog, cat, and pig CYP2Js likely play roles as drug-metabolizing enzymes in the small intestine, similar to human CYP2J2.

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 - 1) Effect of the locational relationship between the 1st wave dominant follicle and the corpus luteum on conception rate after embryo transfer: data analysis of 297 embryo transfers from a commercial embryo production program.

Goto, A., Hayama, K., Urakawa, M., Oono, Y., Hazano, K., Kayano, M., Haneda, S., **Nakada, K.**, Matsui, M.

Journal of the Hellenic Veterinary Medical Society, 73(1), 3635-3640. 2022. doi:10.12681/jhvms.25366

J HELLENIC VET MED SOC 2022, 73 (1): 3635-3640 IIEKE 2022, 73 (1): 3635-3640

Effect of the locational relationship between the 1st wave dominant follicle and the corpus luteum on conception rate after embryo transfer: data analysis of 297 embryo transfers from a commercial embryo production program

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ABSTRACT: The ovarian structures identified at the time of ET are important for the selection of recipients. In previous report, the first-wave dominant follicle, located ipsilateral to the corpus luteum on the ovary, was associated with reduced conception rate after artificial insemination. Thus, a similar locational relationship may affect conception rate during embryo transfer. Data from 297 transfers of fresh embryos to virgin heifers were analyzed aiming to check the effect of first-wave dominant follicle location in relation to the corpus luteum on conception rate using a multivariable logistic regression model with six confounders. The location of the first-wave dominant follicle in relation to the corpus luteum location had no significant effect on conception rate, suggesting that it is not necessary to consider the first-wave dominant follicle size and location in the ovaries for recipient selection.

Keywords: corpus luteum; embryo transfer; first-wave dominant follicle; ipsilateral; recipient

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- I. 筆頭または責任著者 <First or Corresponding Author>
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II. その他<Others>

 Uchida, L., Sakurai, Y., Shimooka, M., Morales-Vargas, R. E., <u>Hagiwara, K.</u>, Muramatsu, Y. (2022). Identification of three novel genes in Phenuiviridae detected from Aedes mosquitoes in Hokkaido, Japan. *Japanese Journal of Infectious Diseases*. DOI: 10.7883/yoken.JJID.2022.179

ORIGINAL ARTICLE

Microbiology and Immunology

Anti-inflammatory effect a specific Lactiplantibacillus plantarum in an ovalbumin-induced asthma model

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Abstract

Autoimmune, allergic, and respiratory inflammatory diseases are some of the most important health issues worldwide. Disorders of the gut microbiota have been associated with the induction of allergic and inflammatory diseases, and probiotics are being tested for disease prevention. We examined functional Lactiplantibacillus plantarum RGU (Lp-1) to mice with ovalbumin (OVA)-induced asthma model to elucidate the inhibitory effect on pathological progression in asthma model. Prior to the experiments, the intestinal lactic acid bacteria were reduced by administering multiple antibiotics (MAB) to evaluate the administration effect of lactic acid bacteria. Mice were administered with Lp-1 or comparative control lactic acid bacteria in each group. After that, OVA-induced asthma was induced, and cytokine gene expression and histological findings were compared. Exacerbation of lung lesions was confirmed in the MAB group. The Lp-1 group mice had alleviated lung lesions with a decrease in IL-13, IL-13, IL-17 and an increase in IL-10 of the splenocytes and bronchial lymph nodes compared with the MAB group, but not in the other groups. In OVA-induced asthma, administration of specific Lactiplantibacillus was confirmed to induce anti-inflammatory cytokines.

KEYWORDS

anti-inflammation, asthma, Lactiplantibacillus

筆頭著者:岸田茂史・最終責任者:萩原克郎; doi: 10.1111/1348-0421.13014

RESEARCH Open Access

Stability of enveloped and nonenveloped viruses in hydrolyzed gelatin liquid formulation

Francois Marie Ngako Kadji^{1*}, Kazuki Kotani¹, Hiroshi Tsukamoto¹, Yosuke Hiraoka¹ and Katsuro Hagiwara^{2*}

Abstract

Background: The thermal stability of viruses in gelatin liquid formulations for medical research and application is poorly understood and this study aimed to examine the thermal stability of 4 enveloped and nonenveloped DNA and RNA viruses in hydrolyzed gelatin liquid formulations.

Methods: Bovine herpesvirus (BHV) was used as a model virus to examine the molecular weight (MW), concentration and gelatin type and to optimize virus stability in liquid formulations at 25 °C and 4 °C. Using the model virus liquid formulation, the stability of multiple enveloped and nonenveloped RNA and DNA viruses, including parainfluenza virus, reovirus (RV), BHV, and adenovirus (AdV), was monitored over up to a 30-week storage period.

Results: The BHV model virus was considered stable after 3 weeks in hydrolyzed gelatin (MW: 4000) with a 0.8 LRV (log10 reduction value) at 25 °C or a 0.2 LRV at 4 °C, compared to the stabilities observed in higher MW gelatin (60,000 and 160,000) with an LRV above 1. Based on the gelatin type, BHV in alkaline-treated hydrolyzed gelatin samples were unexpectantly more stable than in acid-treated hydrolyzed gelatin sample. All four viruses exhibited stability at 4 °C for at least 8 weeks, BHV or AdV remained stable for over 30 weeks of storage, and at 25 °C, AdV and RV remained stable for 8 weeks.

Conclusion: The results demonstrated that 5% of 4000 MW hydrolyzed gelatin formulation can act as a relevant stabilizer for the thermal stability of viruses in medical research and application.

Keywords: Virus, Temperature, Stability, Hydrolyzed gelatin, Formulation

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> Jpn J Infect Dis. 2022 Sep 30. doi: 10.7883/yoken.JJID.2022.179. Online ahead of print.

Identification of three novel genes in Phenuiviridae detected from Aedes mosquitoes in Hokkaido, Japan

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Affiliations + expand

PMID: 36184398 DOI: 10.7883/yoken.JJID.2022.179

Free article

Abstract

Mosquitoes are an important arthropod vector of arboviruses. Family Phenuiviridae includes several medically important arboviruses, such as Rift Valley fever phlebovirus and Toscana phlebovirus. Recent comprehensive genetic analyses identified many novel mosquito-specific viruses that are phylogenetically related to Phenuiviridae. We collected mosquitoes in Hokkaido, northern Japan, and conducted reverse transcription polymerase chain reactions (RT-PCRs) targeting the RNA-dependent RNA polymerase (RdRp) gene of Phenuiviridae. A total of 285 pools comprising 3,082 mosquitoes from two genera and eight species were collected. Partial RdRp sequences were detected from 97 pools, which allowed us to classify the viruses into three clusters provisionally designated Etutanne virus (ETTV) 1, 2, and 3. The closest related virus was Narangue virus (family Phenuiviridae, genus Mobuvirus), which was detected from Mansonia mosquitoes, and the similarities of its nucleotide and amino acid sequences with those of the ETTVs were 58.4%-66.2% and 64.7%-86.7%, respectively. PCRs and RT-PCRs using DNA and RNase digestion methods showed that the ETTVs were RNA viruses, but they do not form non-retroviral integrated RNA virus sequences in the mosquito genome.

Keywords: Aedes; Hokkaido; Mosquito; Phenuiviridae.

筆頭著者:内田玲麻、最終責任者:萩原克郎, doi: 10.7883/yoken.JJID.2022.179

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GENOME SEQUENCES April 2022 Volume 11 Issue 4 e00042-22 https://doi.org/10.1128/mra.00042-22

Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

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ABSTRACT Bovine pneumonia is a disease that causes significant economic losses in livestock industries and is vital for animal welfare. The whole-genome sequence of *Pasteurella multocida* strain Pm1, isolated from a calf suffering from pneumonia in Japan, is reported here.

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最終責任者 Hidetoshi Higuchi (Corresponding Author)



SHORT COMMUNICATION

Experimental Research

Comparing chemiluminescent response and intracellular bactericidal activity of bovine blood neutrophils and monocytes against Salmonella Dublin and Escherichia coli

Hideyasu Satoh¹⁾, Satoshi Gondaira¹⁾, Hidetoshi Higuchi^{1,*)}, Hiromi Ueda²⁾, Masakatsu Nohara³⁾ and Hajime Nagahata^{3,*)}

Received for publication, Mar 7, 2022; accepted, May 15, 2022

Abstract

Chemiluminescent (CL) response and the intracellular killing activity of polymorphonuclear neutrophils (PMNs) and monocytes (MOs) from healthy calves were evaluated to clarify the responsiveness of phagocytes to Salmonella Dublin (S. Dublin) and Escherichia coli (E. coli). CL responses of PMNs and MOs against S. Dublin and E. coli were significantly lower (P < 0.05) than that with opsonized zymosan. The intracellular bactericidal activity of PMNs and MOs was found to be effective against E. coli but not against S. Dublin. These findings indicated that the bactericidal activity of bovine PMNs and MOs against S. Dublin was impaired in innate immune response and that a decreased killing activity against S. Dublin could be a contributing factor for chronic salmonellosis in cattle.

Key Words: bovine monocytes, intracellular bactericidal activity, Salmonella Dublin

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http://hdl.handle.net/2115/86525

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ORIGINAL PAPER



A novel polymerase chain reaction assay for the detection of seven Mycoplasma species of cattle origin

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Abstract

The study aimed to develop a pair of polymerase chain reaction primers for detecting ruminant mycoplasma pathogens. We designed a set of primers based on the most similar sequences within 16 S rRNA regions of seven *Mycoplasma* spp. These primers have high sensitivity for detecting *Mycoplasma dispar*, *M. arginine*, *M. canadense*, *M. bovis*, *M. alkalescens*, *M. californicum*, and *M. bovigenitalium* within the annealing temperature range of 46 to 48 °C. The minimum amount of DNA that can be detected using the protocol is 250 ng, which is equivalent to 2,000 colony-forming units per mL. The primers can detect mycoplasma from DNA extracted directly from milk samples. The common bovine mastitis pathogens of *Staphylococcus aureus* coagulase-negative staphylococci, *Escherichia coli*, *Streptococcus uberis*, *Klebsiella pneumonia*, and *Kocuria rosea* were not detected by the primers. We believe the high sensitivity and specificity of these primers make them useful for detecting infection with seven *Mycoplasma* species in ruminants, allowing the primers to be used in clinical settings.

Keywords Mycoplasma · Polymerase chain reaction · Bovine

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最終責任者 Jyhmirn Lai (First Author and Corresponding Author)

RESEARCH ARTICLE



Evaluation of the health status of mammary glands and compositional changes in udder-half milk obtained from dairy goats for milk quality management

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Abstract

This study evaluated the health status of the mammary glands and milk composition of dairy goats. The California mastitis test (CMT) score, somatic cell counts (SCCs), somatic cell type, electrical conductivity (EC), N-acetyl-β-p-glucosaminidase (NAGase) activity, mastitis-causing pathogens, and milk composition in 121 udderhalf milk samples from 62 crossbreed goats (1-3 years old) at 23-45 days postpartum were compared in four categories with SCCs of <200 × 103, $<300 \times 10^{3}$, $301-1000 \times 10^{3}$, and $>1010 \times 10^{3}$ cells/ml. The SCC, CMT score, EC, and NAGase activity were significantly lower (p < 0.05) in udder-half milk with SCCs of $<200 \times 10^3$ and $<300 \times 10^3$ cells/ml than those in milk with SCCs of 301- 1000×10^3 and >1010 \times 10³ cells/ml. The protein, lactose/ash, and solids-not-fat (SNF) in milk with an SCC of $<300 \times 10^3$ cells/ml were similar to the previously reported values. The proportion of polymorphonuclear neutrophils was significantly higher (p < 0.05) in milk with SCCs of 301–1000 and >1010 \times 10³ cells/ml than in milk with an SCC of <300 × 103 cells/ml. Assessing mammary gland health and milk composition based on categorization of udder-half milk by SCC may be useful for milk quality control on goat farms.

dairy goat, mammary health parameters, milk composition, quality control

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scientific reports



OPEN Biological properties of Staphylococcus virus ΦSA012 for phage therapy

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Staphylococcus virus ФSA012 has a wide host range and efficient lytic activity. Here, we assessed the biological stability of ФSA012 against temperature, freeze-thawing, and pH to clinically apply the phage. In addition, inoculation of ФSA012 through i.p. and i.v. injections into mice revealed that phages were reached the limit of detection in serum and accumulated notably spleens without inflammation at 48 h post-inoculation. Furthermore, inoculation of ФSA012 through s.c. injections in mice significantly induced IgG, which possesses neutralizing activity against ФSA012 and other Staphylococcus viruses, ФSA039 and ФMR003, but not Pseudomonas viruses ФS12-3 and ФR18 or Escherichia viruses T1, T4, and T7 in vitro. Immunoelectron microscopic analysis showed that purified anti-phage IgG recognizes the long-tail fiber of staphylococcus viruses. Although S. aureus inoculation resulted in a 25% survival rate in a mouse i.p. model, ФSA012 inoculation (i.p.) improved the survival rate to 75%; however, the survival rate of ФSA012-immunized mice decreased to less than non-immunized mice with phage i.v. injection at a MOI of 100. These results indicated that OSA012 possesses promise for use against staphylococcal infections but we should carefully address the appropriate dose and periods of phage administration. Our findings facilitate understandings of staphylococcus viruses for phage therapy.

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教授 蒔田 浩平

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Use of a participatory method for community-based brucellosis control design in agropastoral areas in Tanzania.

Asakura S, Makingi G, John K, Kazwala R, Makita K.

Front. Vet. Sci. 9: 767198. 2022. https://doi.org/10.3389/fvets.2022.767198

2) Spatio-temporal epidemiology of animal and human rabies in northern South Africa between 1998 and 2017.

Mogano K, Suzuki T, Mohale D, Phahladira B, Ngoepe E, Kamata Y, Chirima G, Sabeta C, Makita K.

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3) The impact of coronavirus disease 2019 in Japanese companion animal clinics. Fukumoto F, Kimura Y, Tsutsumi A, Hori A, Tanaka A, Ukita M, Makita K. *J. Vet. Med. Sci.* 84(8): 1041-1050. 2022.

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Use of a Participatory Method for Community-Based Brucellosis Control Design in Agro-Pastoral Areas in Tanzania

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Brucellosis is widespread in both humans and livestock in many developing countries. The authors have performed a series of epidemiological studies on brucellosis in agropastoral areas in Tanzania since 2015, with the aim of the disease control. Previously, the potential of a community-based brucellosis control initiative, which mainly consisted of the sale of cattle with experience of abortion and vaccinating calves, was assessed as being effective and acceptable based on a quantitative approach. This study was conducted to investigate the feasibility of community-based brucellosis control program using participatory rural appraisals (PRAs) and key-informant interviews. Four PRAs were performed together with livestock farmers and livestock and medical officers in 2017. In the PRAs, qualitative information related to risky behaviors for human infection, human brucellosis symptoms, willingness to sell cattle with experience of abortion, and willingness to pay for calf vaccination were collected, and a holistic approach for a community-based disease control project was planned. All of the communities were willing to implement disease control measures. To avoid human infection, education, especially for children, was proposed to change risky behaviors. The findings of this study showed that community-based disease control measures are promising.

Keywords: agro-pastoralist, brucellosis, disease control, participatory epidemiology, Tanzania

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Data Availability Statement Data on labies diagnoses cannot be shared publicly because they need permission from the Republic of South Africa. Researchers may request access to the data provider. Rurther details on the process for requesting access can be found at ARC-ONDERSTEPOORT VETER INARY RESEARCH (ARC-OVR) https://www.arc.apric.ze/poort-borreage.apx, Genome sequence data are available in GenBank under following accession numbers: AF177105, EF686061, EF686073,

RESEARCH ARTICLE

Spatio-temporal epidemiology of animal and human rabies in northern South Africa between 1998 and 2017

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Abstract

Background

Rabies is a fatal zoonotic disease that is maintained in domestic dogs and wildlife populations in the Republic of South Africa. A retrospective study was conducted to improve understanding of the dynamics of rabies in humans, domestic dogs, and wildlife species, in relation to the ecology for three northern provinces of South Africa (Limpopo, Mpumalanga, and North-West) between 1998 and 2017.

Methods

A descriptive epidemiology study was conducted for human and animal rabies. Dog rabies cases were analyzed using spatio-temporal scan statistics. The reproductive number (R_t) was estimated for the identified disease clusters. A phylogenetic tree was constructed based on the genome sequences of rabies viruses isolated from dogs, jackals, and an African civet, and Bayesian evolutionary analysis using a strict time clock model. Several ecological and socio-economic variables associated with dog rabies were modeled using univariate analyses with zero-inflated negative binomial regression and multivariable spatial analyses using the integrated nested Laplace approximation for two time periods: 1998—2002 and 2008—2012.

Results

Human rabies cases increased in 2006 following an increase in dog rabies cases; however, the human cases declined in the next year while dog rabies cases fluctuated. Ten disease clusters of dog rabies were identified, and utilizing the phylogenetic tree, the dynamics of

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FULL PAPER

Epidemiology

The impact of coronavirus disease 2019 (COVID-19) in Japanese companion animal clinics

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ABSTRACT. The coronavirus disease 2019 (COVID-19) pandemic has had a tremendous impact on people's lives throughout the world. A cross-sectional study was conducted to clarify the influence of COVID-19 on Japanese companion animal clinics, A self-administered electronic questionnaire regarding the incidence of COVID-19, hygiene management, the influence on clinical service and employment, and mental stress of staff was conducted for workers in animal clinics between 1 May and 10 June 2021. Questions concerning the hygiene management before the occurrence of COVID-19, under the first state of emergency, and at the time of the survey were asked using the Likert scale. Kessler 6 (K6) was used as an indicator of mental distress. In total, 430 individuals responded. Of these, 4.9% experienced COVID-19 infection in staff. Hygiene management was strengthened, but no particular practice was statistically associated with the occurrence of COVID-19 cases in staff. In Nakaya's variation of Scheffe's paired comparison, the highest prioritized goal in the clinics was the prevention of nosocomial infection with COVID-19. The prevalence of serious mental illness (K6 >=13) was 11.1% (95% confidence interval: 6.3-18.6%). Multivariable negative binomial regression found four risk factors for psychological distress: veterinary nurse (P=0.016 with veterinarians and P<0.01 with other staff), female (P=0.004), fear of infection at work (P<0.001), and stress by refraining from going out (P<0.001). Directors of clinics are recommended to take care of female veterinary nurses for distress.

KEYWORDS: companion animal clinic, coronavirus disease 2019, hygiene management, mental health, veterinary nurse

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ORIGINAL ARTICLE

WILEY

The final stages of dog rabies elimination from Japan

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Abstract

Rabies is a lethal zoonotic disease mainly transmitted to humans by dog bites. The purpose of this study was to assess the efficacy of rables control policies in Japan, which resulted in the elimination of the disease from the country in 1957. Using historical records from the Kanto region (Chiba, Kanagawa, Saitama and Tokyo Prefectures) between 1947 and 1956 where the final canine cases were recorded, we undertook a descriptive epidemiological study, applying spatio-temporal scan statistics using SaTScan and estimating the effective reproduction number (R₊) for the clusters and each prefecture using the growth rates. There were 1,567 dog rabies and 161 human rabies cases recorded during this period. Vaccination coverage in registered dogs was over 70% after 1951, with much lower coverage in free-roaming and unregistered dogs. Eight clusters of dog rabies cases were identified: the first appeared in 1947 in Tokyo and was linked to three further clusters in peripheral prefectures between 1947 and 1951. Three more clusters occurred in Tokyo again between 1952 and 1954, and the last cluster was in Tokyo and Kanagawa between 1955 and 1956. R, in the first cluster was 1.68, and R, values in the others ranged between 1.18 and 1.86, with an exception of 4.05 in the smallest cluster in Tokyo in 1952 (10 cases). The moving average of R, coincided with the clusters. As dog vaccination and dog management progressed, and the number of dog rabies cases declined, the moving average of R, declined to below 1. Delays in the implementation of dog management policies in Kanagawa may have prolonged this last outbreak. These results demonstrate the effectiveness of coordinated control policy involving dog vaccination and management of free-roaming dog populations for rabies elimination.

KEYWORDS

basic reproduction number, effective reproduction number, rabies, spatio-temporal cluster

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Economic losses associated with mastitis due to bovine leukemia virus infection

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ABSTRACT

Bovine leukemia virus (BLV), which causes enzootic bovine leukosis and immunosuppression, is widely prevalent on Japanese dairy farms. However, in the absence of a national eradication scheme with compensation programs, it is important to estimate BLV-associated economic losses to raise farmers' awareness. Mastitis (includes both clinical and subclinical) is a common disease in the dairy industry and the most common reason for culling. We hypothesized that immunosuppression due to BLV predisposes subclinical mastitis. A retrospective cohort study was conducted to trace Holstein cows at 9 commercial dairy farms in the Nemuro and Kushiro regions of Hokkaido Prefecture, Japan, where monitoring of BLV proviral load is routine. Information regarding Dairy Herd Improvement data, parity number, and delivery day was collected at each farm. Cows with no confirmed infection with BLV during lactation were defined as non-infected. Low-proviral-load and high-proviral-load (H-PVL) cows were defined as those in which proviral load was below and over 2,465 copies/50 ng of DNA, respectively, or 56,765 copies/10⁵ cells, respectively, throughout the lactation period. Survival analysis was performed using the frailty model to estimate the hazard ratio of subclinical mastitis for BLV infection status using data from 1,034 dairy cows after adjusting for parity number and delivery season as confounding factors. Kaplan-Meier survivor curves demonstrated that half of the H-PVL cows developed subclinical mastitis within 52 d after calving. The hazard ratio of subclinical mastitis for H-PVL cows was 2.61 times higher than that of non-infected cows. In 2017, there were 264,443 clinical mastitis cases in Hokkaido. Using field and published data, annual economic losses were estimated using Monte Carlo simulation. The economic loss due to mastitis associated with BLV infection per H-PVL cow was \$418.6 (¥43,952). with the annual economic loss in Hokkaido Prefecture due to mastitis caused by BLV infection estimated at \$6,097,225 (¥640,208,633). In summary, H-PVL cows were more susceptible to subclinical mastitis than noninfected and low-proviral-load cows, and mastitis due to BLV infection was projected to cause significant economic losses.

Key words: bovine leukemia virus, mastitis, survival analysis, economic loss

INTRODUCTION

Bovine leukemia virus (BLV) belongs to the genus Deltaretrovirus of the family Retroviridae and is related to several clinically important viruses, such as human T-cell lymphotropic virus type 1 and 2 and simian Tcell lymphotropic virus type 1 and 2 (El Hajj et al., 2012). Bovine leukemia virus causes enzootic bovine leukosis (EBL) in cattle, leading to significant economic losses (Rodríguez et al., 2011; Bartlett et al., 2020). Bovine leukemia virus is prevalent worldwide, except in Western Europe (OIE, 2018). Most infections are subclinical, but a proportion of cattle (<30%) over 3 yr old develop persistent lymphocytosis, and less than 5% of infected cattle develop lymphosarcomas in various visceral tissues (EFSA, 2015). Clinical signs and symptoms depend on tumor site and include digestive disturbances, inappetence, weight loss, weakness, general debility, and sometimes neurologic manifestations (OIE, 2018).

The BLV infection has a significant economic impact on the dairy industry due to trade restrictions, replace-

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Key words:

Black-backed jackal; C. mesomelos; crossspecies transmission; Lyssaviruses; rabies; South Africa

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Rabies outbreak in black-backed jackals (Canis mesomelas), South Africa, 2016

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Abstract

Rabies, a fatal and vaccine-preventable disease, is endemic throughout Africa. In 2016, a rabies outbreak occurred in black-backed jackals (Canis mesomelas) along the western boundary of Gauteng Province, South Africa. We investigated the possible drivers of the 2016 outbreak and established its origin. Using spatio-temporal locations of cases, we applied logistic regression and Geographic Information System techniques to investigate environmental covariates driving occurrences of emerging rabies cases in Gauteng Province. About 53.8% of laboratoryconfirmed lyssaviruses in Gauteng Province in 2016 originated from jackals. Phylogenetic trees reconstructed from a partial region of the glycoprotein gene of these and historical rabies viruses (RABVs) demonstrated the lyssaviruses to be of canid origin with 97.7% nucleotide sequence similarity. The major cluster comprised jackal RABVs from the 2012 KwaZulu/ Natal outbreak and the 2016 outbreak in Gauteng Province. The second cluster was composed of both jackal and dog RABVs. Both clusters correlated with independent RABV introductions into Gauteng by dogs and jackals, respectively. This study demonstrated an expansion of a jackal rabies cycle from north-west Province into Gauteng Province during the 2016 dry period, as jackals ranged widely in search for food resources leading to increased jackal-dog interactions, reminiscent of the intricate links of domestic and wildlife rabies cycles in South Africa.

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Healthy Aging: Comparative Analysis of Local Perception and Diet in Two Health Districts of Côte d'Ivoire and Japan

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Context: Good health and longevity depend on dynamic interactions between biological, social, psychological, and environmental factors. Aging is globally a big challenge, particularly with the demographic transition, including population growth, and an emerging burden to society. Knowledge, behavior, diet, and consumption of animal source food were related to aging and emerged as the key factors modulating healthy aging.

Objective: The study was designed to understand the main healthy aging factors, such as knowledge, social network, and diet of elders, and to derive mutual learning from it for healthy aging.

Methods: A qualitative approach has been applied to explore health-related knowledge, attitude, and diet of elders from Ebetsu (Japan) and Tiassalé (Côte d'Ivoire) health districts, using focus group discussions and comparative context analysis between high- and low-income, contries

Results: The study shows that living longer is a common feature of people in Japan compared to Côte d'Ivoire, where the life expectancy is still low. Both groups of elders have social networks that support them, and both offer their gained experience to society. While Japanese elders depend on pension and insurance for income and medical treatments, livorians depend mostly on their children and social network in old age. The worries of elders differ between the two regions. In Ebetsu, elder members of the community are concerned about the future burden they pose for the younger generation if they develop illhealth, making them more resilient to aging. In Taabo, elders are considered to be culturally and socially useful to the society. Elders in Ebetsu pointed out that for healthy aging, education on diet at a younger age, physical activities, and access to basic social services are the key aspects. This was not observed in Taabo's context. Being inactive and dependent on others were described as the most worrying situations for elders in Ebetsu, as it is perceived to increase the risk of non-communicable diseases and anxiety. Elders in Ebetsu have good knowledge on what constitutes a healthy diet, and they believe that

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Decreasing the abundance of tetracycline-resistant *Escherichia coli* in pig feces during nursery using flavophospholipol as a pig feed additive

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ARTICLEINFO

Keywords: Tetracycline resistance Flavophospholipol Escherichia coli Pig Conjugational transfer

ABSTRACT

Tetracyclines (TCs) are widely used for livestock, and the high prevalence of TC-resistant Escherichia coli in livestock has become a serious concern worldwide. In Japan, the National Action Plan on Antimicrobial Resistance in 2016 aimed to reduce the TC resistance rate in E. coli derived from livestock. Flavophospholipol (FPL), used as a feed additive, has an inhibitory effect on the spread of plasmid-mediated antimicrobial resistance. The number of TC-resistant E. coli was determined in pigs administered TCs and/or FPL to clarify the effect of FPL on reducing the number of TC-resistant E. coli in pigs. TC-resistant E. coli and their plasmids were then analyzed. The pigs were divided into four groups: control, doxycycline (DOXY; a TC), FPL, and a DOXY-FPL combination. Their feces were collected from the nursing period to the day before being transported to the slaughterhouse, followed by estimation of TC-resistant E. coli (colony-forming units [CFU]/g). The number of TC-resistant E. coli increased with the use of DOXY, suggesting that DOXY administration provides a selective pressure for TC-resistant E. coli. Supplementation with FPL as a feed additive significantly suppressed the increase in the number of TC-resistant E. coli, especially during the DOXY administration period. Transfer and growth inhibition analyses were performed for TC-resistant isolates. FPL inhibited the conjugational transfer and growth of a few TC-resistant E. coli isolates. These results suggest that FPL is effective against the spread of TC-resistant E. coli.

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Veterinary Emergency AND Critical Care



ORIGINAL STUDY

Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis

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This study was presented in part as a poster presentation at the 13th World Congress of Veterinary Anaesthesiology, Venice, Italy, September 2018.

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Abstract

Objective

Acidosis decreases myocardial contractile and myofibrillar responsiveness by reducing the calcium sensitivity of contractile proteins, which could reduce the effectiveness of pimobendan. We aimed to assess the cardiovascular effects of pimobendan in dogs subjected to acute respiratory acidosis.

Design

Randomized crossover study with a 2-week washout period.

Setting

University Laboratory.

Animals

Six healthy research Beagle dogs.

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 - 1) Nishi K, Hirano Y, Sato A, Eguchi A, <u>Matsuda K</u>, Toda M, Watanabe T, Iwasaki T, Takahashi N, Hosotani M, Watanabe R, Kato T, Ohtsuka H, Gondaira S, Higuchi H. Effects of intra-articular inoculation with *Mycoplasma bovis* on immunological responses in calf joints. *Vet Immunol Immunopathol.* **244**: 110364. 2022. doi.org/10.1016/j.vetimm.2021.110364.

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Veterinary Immunology and Immunopathology





Research paper

Effects of intra-articular inoculation with Mycoplasma bovis on immunological responses in calf joints

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ARTICLE INFO

Keywords: Arthritis Inflammatory cytokines Invasion Matrix metalloproteinases

ABSTRACT

Mycoplasma arthritis that caused by Mycoplasma bovis exhibit severe lameness. This disease is difficult to cure with antibiotics, but the detailed pathological mechanisms have not been fully clarified. In this study, we examined the effects of intra-articular inoculation with M. bovis on immunological responses in calf joints. We inoculated three calves each with M. bovis or phosphate buffer saline (control) into the right stifle joint and dissected them at 15 days postinoculation. Mycoplasma bovis-inoculated calves exhibited swelling of the stifle joint, increases in synovial fluid, fibrin deposition, and cartilage thinning. Intracellular M. bovis was detected in synovial tissues analyzed by immunohistochemistry and transmission electron microscopy. Messenger RNA expressions of interleukin (IL)-1β, IL-6, IL-8, IL-12p40, and IL-17A in synovial fluid cells and synovial tissues from M. bovis-inoculated calves were significantly higher than those from control calves. Protein levels of these cytokines in synovial fluid from M. boxis-inoculated calves were markedly higher than those from control calves. Our study clarified that inoculation with M. bovis into the stifle joint induced the production of inflammatory cytokines by synovial fluid cells and synovial tissues, causing a severe inflammatory response in joints. Additionally, M. bovis could invade cells in synovial tissues, which may have aided it in evading antibiotics and host immune surveillance.

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Cryptosporidium sp. Mrb001 detected from Myodes rufocanus bedfordiae, an indigenous vole of Hokkaido, Japan

MuramatsuY, Uchida L, Tamura Y, Asakawa M.

Bull. Rakuno Gakuen Univ. Nat. 46: 45-48. 2022.

- II. その他<Others>
- 1) Identification of three novel genes in *Phenuiviridae* detected from **Aedes** mosquitoes in Hokkaido, Japan.

Uchida L, Sakurai Y, Shimooka M, Morales-Vargas RE, Hagiwara K,

MuramatsuY

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Cryptosporidium sp. Mrb001 detected from Myodes rufocanus bedfordiae, an indigenous vole of Hokkaido, Japan

Yasukazu Muramatsu¹*, Leo Uchida¹, Yutaka Tamura², and Mitsuhiko Asakawa³

ABSTRACT. Cryptosporidium oocysts were detected from five of 111 grey red-backed voles (Myodes rufocanus bedfordiae) in a forestry area of Hokkaido, which is the northernmost island of Japan and is zoogeographically distinct from the mainland. The number of oocysts per gram of faeces from each vole ranged from 1.5×10^6 to 1.8×10^8 . A partial sequence of small subunit 18S rDNA (SSU rDNA) obtained in this study was registered as Cryptosporidium sp. Mrb001 (GenBank accession no. AB477098) and had the highest similarity to Cryptosporidium sp. 05.1513.Rb (GenBank accession no. HM015880.1), which originated from drinking water in the United Kingdom (98.5%). Phylogenetic tree analysis indicated that Cryptosporidium sp. Mrb001 clustered with several waterborne Cryptosporidium isolates and other Cryptosporidium spp. that originated from voles that inhabit wetlands in Hokkaido. We provided information about this cryptosporidial parasite isolated from Myodes vole. (139 words)

KEYWORDS: Cryptosporidial parasite, small rodent, wetland, small subunit 18S rDNA

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Identification of three novel genes in *Phenuiviridae* detected from *Aedes* mosquitoes in Hokkaido, Japan

Leo Uchida, Yoshimi Sakurai, Makoto Shimooka, Ronald Enrique Morales-Vargas, Katsuro Hagiwara, and Yasukazu Muramatsu

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- 1) Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs.

Chen IY, Tamogi H, Wei Y, Kato K, Itami T, Sano T, <u>Yamashita K.</u> *Vet Anaesth Analg.* 49:36-44. 2022. doi: 10.1016/j.vaa.2021.10.002.

II. その他<Others>

1) Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits.

Wei Y, Hori A, Chen IY, Tamogi H, Hirokawa T, Kato K, Itami T, Sano T, <u>Yamashita</u> K.

J Vet Med Sci. 84:792-798. 2022. doi: 10.1292/jvms.21-0648.

2) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia.

Hanazono K, Nakamoto M, Hori A, Miyoshi K, Nakade T, Itami T, Sano T, Kato K, Ito A, Tanaka K, <u>Yamashita K</u>, Endoh D.

J Vet Med Sci. 84:1556-1562. 2022. doi: 10.1292/jvms.22-0122.

3) Sparing effect of tramadol, lidocaine, dexmedetomidine and their combination on the minimum alveolar concentration of sevoflurane in dogs.

El-Hawari SF, Oyama N, Koyama Y, Tamura J, Itami T, Sano T, <u>Yamashita K.</u> *J Vet Sci.* 23:e53. 2022. doi: 10.4142/jvs.21305.

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Peer J. 10:e13134. 2022. doi: 10.7717/peerj.13134.

RESEARCH PAPER

Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs

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Abstract

Objective To compare the effects of sevoflurane, propofol and alfaxalone on the neuromuscular blockade induced by a single intravenous bolus of rocuronium in dogs.

Study design A randomized, prospective, crossover experimental study.

Animals A total of eight adult Beagle dogs (four female, four male), weighing $8.9{-}15.3~{\rm kg}$ and aged $5{-}7~{\rm years}$.

Methods The dogs were anesthetized three times with $1.25\times$ minimum alveolar concentration of sevoflurane (SEVO treatment) and $1.25\times$ minimum infusion rate of propofol (PROP treatment) or alfaxalone (ALFX treatment) at intervals of $\geq \! 14$ days. Neuromuscular function was monitored with train-of-four (TOF) stimulation of the peroneal nerve by acceleromyography. After recording the control TOF ratio (TOFRC), a single bolus dose of rocuronium (1 mg kg $^{-1}$) was administered intravenously. The times from rocuronium administration to achieving TOF count 0 (onset time), from achieving TOF count 0 to the reappearance of TOF count 4 (clinical blockade period), from 25% to 75% of TOFRC (recovery index) and from achieving TOF count 0 to TOF ratio/TOFRC >0.9 (total neuromuscular blockade duration) were recorded.

Results The onset time and recovery index did not differ among the treatments. The median clinical blockade period was longer in the SEVO treatment [27.3 (26.0–30.3) minutes] than in PROP [16.6 (15.4–18.0) minutes; p=0.002] and ALFX [22.4 (18.6–23.1) minutes; p=0.017] treatments; and longer in the ALFX treatment than in the PROP treatment (p=0.020). The mean total neuromuscular blockade duration was longer in the SEVO treatment

 $(43.7 \pm 9.9 \text{ minutes})$ than in PROP $(25.1 \pm 2.7 \text{ minutes}; p < 0.001)$ and ALFX $(32.5 \pm 8.4 \text{ minutes}; p = 0.036)$ treatments.

Conclusions and clinical relevance Compared with alfaxalone and propofol, sevoflurane prolonged rocuroniuminduced neuromuscular blockade by a significantly greater extent in dogs.

Keywords alfaxalone, dogs, neuromuscular blockade, propofol, rocuronium, sevoflurane.

Introduction

Rocuronium bromide, an aminosteroid, is a nondepolarizing neuromuscular blocking agent (NMBA). It has a faster onset as compared with that of vecuronium, but the duration of action is similar between the two (Marshall et al. 1994; Larijani et al. 1995; Kansanaho et al. 1997). Currently, rocuronium has widespread clinical application in veterinary practice and has been administered to dogs through intravenous (IV) boluses, incremental IV doses or constant rate infusion (CRI) to improve skeletal muscle relaxation during surgical procedures under general anesthesia (Dugdale et al. 2002; Alderson et al. 2007; Auer et al. 2007; Briganti et al. 2015; Haga et al. 2019).

However, administration of NMBAs may lead to a residual block, which is the presence of a neuromuscular blockade during the postoperative period (Jones et al. 2015). Studies in humans have shown that sex, body weight, body temperature, concentration of volatile anesthetic agents and interval between the last NMBA administration and reversal agent administration are associated with a residual block (Vanlinthout et al. 1996; Srivastava & Hunter 2009; Khamtuikrua et al. 2017; Saager et al. 2019).

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Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits

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ABSTRACT. Recently, a mucosal atomization device (MAD) has been applied in veterinary medicine. In the present study, the maximum volume of nasal atomization without aspiration using MAD was examined in eight healthy female Japanese White (JW) rabbits. Each rabbit had their head and neck examined by computed tomography before and after nasal atomization with four different doses (0.15, 0.3, 0.45, and 0.6 ml per nostril) of diluted contrast medium (1:2 mixture of lohexol and saline). This was done under general anesthesia by an intramuscular administration of alfaxalone 2.5 mg/kg, medetomidine 40 µg/kg, and butorphanol 0.4 mg/kg, with a 7-day washout period between each treatment. The diluted contrast medium was distributed in the nasal cavity, external nares, and/or oral cavity in all rabbits receiving each treatment. The intranasal distribution volumes of the contrast medium were 287 (250-333) mm³ [median (interquartile range)) for 0.15 ml, 433 (243-555) mm³ for 0.3 ml, 552 (356-797) mm³ for 0.45 ml, and 529 (356-722) mm3 for 0.6 ml of treatment. The intranasal distribution volume for 0.15 ml treatment tended to be lower than that for 0.6 ml treatment (P=0.083). The contrast medium was deposited in the trachea in one rabbit (12.5%) and four rabbits (50%) receiving treatments of 0.45 and 0.6 ml per nostril, respectively. The maximum volume of nasal atomization without aspiration into the trachea was 0.3 ml per nostril for the JW rabbits.

KEYWORDS: intranasal administration, mucosal atomization device (MAD), nasal atomization volume, rabbit

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9246693/pdf/jvms-84-792.pdf

最終責任者 Ai Hori (Corresponding Author)

The Journal of Veterinary Medical Science



FULL PAPER

internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC₃/Ao) and the ratio of long to short diameter of the CVC (CVC₄/CVC₃) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₃/Ao and MBP, in contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₃/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC₃/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/CVC₃ of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₃/Ao of the thorax, CVC₄/CVC₅ of the thorax, CVC₄/Ao of the abdomen, and CVC₁/CVC₅ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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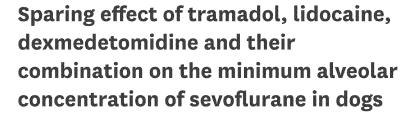
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Original Article Anesthesiology





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ABSTRACT

Background: Problems associated with using inhalational anaesthesia are numerous in veterinary anaesthesia practice. Decreasing the amount of used inhalational anaesthetic agents and minimising of cardiorespiratory disorders are the standard goals of anaesthetists. Objective: This experimental study was carried out to investigate the sparing effect of intravenous tramadol, lidocaine, dexmedetomidine and their combinations on the minimum alveolar concentration (MAC) of sevoflurane in healthy Beagle dogs.

Methods: This study was conducted on six beagle dogs. Sevoflurane MAC was determined by the tail clamp method on five separate occasions. The dogs received no treatment (control; CONT), tramadol (TRM: 1.5 mg kg¹ intravenously followed by 1.3 mg kg¹ h¹), lidocaine (LID: 2 mg kg¹ intravenously followed by 3 mg kg¹ h¹), dexmedetomidine (DEX: 2 μ g kg¹ intravenously followed by 2 μ g kg¹ h¹), and their combination (COMB), respectively. Cardiorespiratory variables were recorded every five minutes and immediately before the application of a noxious stimulus.

Results: The COMB treatment had the greatest sevoflurane MAC-sparing effect (67.4 \pm 13.9%) compared with the other treatments (5.1 \pm 25.3, 12.7 \pm 14.3, and 40.3 \pm 15.1% for TRM, LID, and DEX treatment, respectively). The cardiopulmonary variables remained within the clinically acceptable range following COMB treatment, although the mean arterial pressure was higher and accompanied by bradycardia.

Conclusions: Tramadol-lidocaine-dexmedetomidine co-infusion produced a remarkable sevoflurane MAC-sparing effect in clinically healthy beagle dogs and could result in the alleviation of cardiorespiratory depression caused by sevoflurane. Cardiorespiratory variables should be monitored carefully to avoid undesirable side effects induced by dexmedetomidine.

Keywords: Dog; Tramadol; Lidocaine; Dexmedetomidine; Anaesthesia

ORIGINAL STUDY



Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis

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This study was presented in part as a poster presentation at the 13th World Congress of Veterinary Anaesthesiology, Venice, Italy, September 2018.

Abstract

Objective: Acidosis decreases myocardial contractile and myofibrillar responsiveness by reducing the calcium sensitivity of contractile proteins, which could reduce the effectiveness of pimobendan. We aimed to assess the cardiovascular effects of pimobendan in dogs subjected to acute respiratory acidosis.

Design: Randomized crossover study with a 2-week washout period.

Setting: University Laboratory.

Animals: Six healthy research Beagle dogs.

Interventions: Anesthetized dogs were administered 2 doses of IV pimobendan during conditions of eucapnia ($Paco_2 35-40 \text{ mm Hg}$) and hypercapnia ($Paco_2 90-110 \text{ mm}$ Hg). Eucapnia was maintained by positive pressure ventilation and hypercapnia was induced by adding exogenous CO₂ to the anesthesia circuit. Heart rate (HR), systemic arterial blood pressure, cardiac output (CO), systemic and pulmonary vascular resistance (SVR and PVR, respectively), and pulmonary arterial pressure (PAP) were measured at baseline and 60 min after administering 0.125 mg/kg (low) and 0.25 mg/kg (high) pimobendan intravenously. Blood gas and biochemical analyses were performed at baseline and at the end of the experiment.

Measurements and Main Results: The median baseline blood pH was 7.41 (range: 7.33-7.45) and 7.03 (range: 6.98-7.09) under conditions of eucapnia and hypercapnia, respectively. The serum concentrations of epinephrine and norepinephrine and the HR, CO, and PAP were higher, and SVR was lower at baseline in hypercapnic dogs. Pimobendan dose-dependently increased CO in eucapnia (baseline: $3.6 \pm 0.2 \text{ L/kg/m}^2$ [mean \pm SE], low: $5.0 \pm 0.4 \,\text{L/kg/m}^2$, high: $5.8 \pm 0.5 \,\text{L/kg/m}^2$, P < 0.001) and hypercapnia (baseline: $4.9 \pm 0.5 \text{ L/kg/m}^2$, low: $5.8 \pm 0.5 \text{ L/kg/m}^2$, high: $6.2 \pm 0.5 \text{ L/kg/m}^2$, P < 0.001), and increased HR and decreased SVR and PVR under both conditions (P < 0.001). In hypercapnia, the degree of increase or decrease of these cardiovascular measurements (except for PAP) by pimobendan was less than that in the eucapnic dogs.

Abbreviations: cAMP, cyclic adenosine monophosphate; CO, cardiac output; HR, heart rate; MAP, mean arterial pressure; mPAP, mean pulmonary arterial pressure; PDE, phosphodiesterase; PAOP, pulmonary artery occlusion pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SVI, stroke volume index; SVR, systemic vascular resistance

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Multilingual validation of the short form of the Unesp-Botucatu Feline Pain Scale (UFEPS-SF)

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ABSTRACT

Background. Pain is the leading cause of animal suffering, hence the importance of validated tools to ensure its appropriate evaluation and treatment. We aimed to test the psychometric properties of the short form of the Unesp-Botucatu Feline Pain Scale (UFEPS-SF) in eight languages.

Methods. The original scale was condensed from ten to four items. The content validation was performed by five specialists in veterinary anesthesia and analgesia. The English version of the scale was translated and back-translated into Chinese, French, German, Italian, Japanese, Portuguese and Spanish by fluent English and native speaker translators. Videos of the perioperative period of 30 cats submitted to ovariohysterectomy (preoperative, after surgery, after rescue analgesia and 24 h after surgery) were randomly evaluated twice (one-month interval) by one evaluator for each language unaware of the pain condition. After watching each video, the evaluators scored the unidimensional, UFEPS-SF and Glasgow composite multidimensional feline pain scales. Statistical analyses were carried out using R software for intra and interobserver reliability, principal component analysis, criteria concurrent and predictive validities, construct validity, item-total correlation, internal consistency, specificity, sensitivity, the definition of the intervention score for rescue analgesia and diagnostic uncertainty zone, according to the receiver operating characteristic (ROC) curve.

Results. UFEPS-SF intra- and inter-observer reliability were ≥0.92 and 0.84, respectively, for all observers. According to the principal component analysis, UFEPS-SF is a unidimensional scale. Concurrent criterion validity was confirmed by the high

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Modified medial patellofemoral ligament reconstruction for severe bilateral congenital patellar luxation in a dog.

Isaka M, Kokubo D and Ueno H.

Open Veterinary Journal 2022; 12(1):1-4. doi: 10.5455/OVJ.2022.v12.i1.1.

2) Comparison of intestinal microbiota between healthy and MMVD Chihuahuas using 16S rRNA gene amplicon sequencing.

Araki R, Iwanaga K, Ueda K, Shima A, Ishihara G, Aizu M, Fukayama T,

Isaka M.

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3) Positive Outcomes after Surgical Correction of Grade IV Medial Patellar Luxation in Small Breed Dogs.

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4) The Leaflet-Annulus Index in Canine Myxomatous Mitral Valve Disease.

Isaka M, Hisada S, Araki R and Ueno H.

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Frontiers in Veterinary Science. 2022; 9: 1008765. doi: 10.3389/fvets.2022.1008765.

6) Superficial digital flexor tendon luxation in a golden retriever.

Isaka M, Yamaguchi M, Kokubo D, Konno W, Ueno H.

Open Veterinary Journal 2022; 12(6): 851-854. doi: 10.5455/OVJ.2022.v12.i6.9

7) Serum Concentrations of Osteoprotegerin/Brain-Derived Nerve Factor/ Angiotensin II/ Endothelin-1 of ageing in dogs.

Isaka M._

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Case Report

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Modified medial patellofemoral ligament reconstruction for severe bilateral congenital patellar luxation in a dog

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Abstract

Background: Lateral patellar luxation (LPL) is commonly diagnosed in large or giant breed dogs. In the surgical outcome for canine LPL, approximately half of the patients had complications, including reoperation and relaxation. Medial patellofemoral ligament (MPFL) reconstruction has been widely used for human repetitive patellar luxation. This case report describes that modified MPFL reconstruction with other surgical techniques might be effective for severe canine LPL repair.

Case Description: An 11-month-old intact male Siberian Husky was referred to us with the main complication reported as bilateral hind lameness and LPL, diagnosed by a family doctor. Physiological examination showed bilateral patellar luxation (grade 4). We performed general surgical techniques with modified MPFL. The patient showed good prognosis.

Conclusion: This report suggests that modified MPFL with general surgical techniques for LPL might be an effective surgical technique in dogs.

Keywords: Dog, Lateral patellar luxation, Modified medial patellofemoral ligament.

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Comparison of Intestinal Microbiota Between Healthy and MMVD Chihuahuas Using 16S rRNA Gene Amplicon Sequencing

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Myxomatous mitral valve disease (MMVD) is the most common cause of congestive heart failure in dogs, and although complications of MMVD to the lungs and kidneys have been identified, complications to the gut are less well understood. The intestinal microbiota is an important factor in the gut, and although the association between heart disease and the intestinal microbiota has been shown in human medicine, it is unknown in dogs. The study aimed to evaluate the relationship between MMVD and gut microbiota. A total of 69 healthy Chihuahuas and Chihuahuas with MMVD were evaluated for cardiac health by echocardiography and chest radiography and grouped according to ACVIM guidelines. Fecal samples were collected from all cases and 16S rRNA sequencing was used to reveal the intestinal microbiota. There were significant differences in LA/Ao, LVIDd, E vel, VHS, and VLAS with the severity of ACVIM. On the other hand, there were no significant differences in the diversity and composition of gut microbiota among the groups. The present study did not identify the effects of MMVD on the gut microbiota.

Keywords: Chihuahua, fractional shortening, intestinal complication, intestinal microbiota, myxomatous mitral valve disease

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Positive outcomes after surgical correction of grade IV medial patellar luxation in small breed dogs

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Abstract

Background: Medial patellar luxation (MPL) is a common orthopedic condition in dogs. After surgical correction, the recurrent rates appear to be higher and outcomes worse in grade IV than in lower grade MPL.

Aim: To describe the outcomes of surgical correction of canine grade IV MPL.

Methods: This retrospective study analyzed the medical records of 16 dogs (11 females, 5 males; mean age = 5.05 years) with 22 stifle joints (8 left and 14 right) that underwent MPL surgery at Rakuno Gakuen University between May 2015 and October 2020. The procedures included capsulorrhaphy, trochlear block recession, tibial tuberosity transposition, medial retinacular release, and lateral fabellotibial suturing. The types of postsurgical complications, including a recurrence of MPL, were recorded.

Results: Twelve of the 16 (75 %) dogs had concurrent contralateral MPL, and 2 dogs (12.5%) had concurrent cranial cruciate ligament rupture. The mean follow-up was 12.1 months. No lameness was observed. The outcomes of surgery for grade IV MPL were not associated with bilateral surgery, age, sex, body weight, or the preoperative quadriceps angle. Although none of the dogs showed any major or catastrophic complications following surgery, postoperative minor and major complications were observed in 8 of the 22 stifle joints (36.4%).

Conclusion: Grade IV MPL is a complex orthopedic disease in dogs, which requires surgical patellar realignment to improve limb function. The surgical techniques used in this study were associated with a good prognosis without a surgical revision.

Keywords: Canine diseases, Cranial cruciate ligament, Medial Patellar Luxation, Outcomes assessment, Postoperative complications.

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The leaflet-annulus index in canine myxomatous mitral valve disease

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Keywords:
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Myxomatous mitral valve disease (MMVD) is the most common chronic heart valve disease, leading to the eccentric hypertrophy. Recently, the leaflet-annulus index (LAI), which focuses on the mitral valve apparatus, has been considered a prognostic factor for human mitral regurgitation (MR); however, it has not been reported in veterinary medicine. In the present study, we retrospectively evaluated the LAI in dogs with MMVD. Eight-three dogs with MMVD diagnosed using echocardiography were included in this study. The anteroposterior length, anterior and posterior cusp coaptation lengths, LAI, left ventricular end-diastolic internal diameter normalized to body weight (LVIDDN), and left atrium to sorta ratio (LA/Ao) were measured. A significant correlation between the LAI, LVIDDN, and LA/Ao of MR grading, and left ventricle dilation was observed. In conclusion, LAI could help determine annular widening, suggesting the decision of an appropriate for SVR in clinical settings.

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COMBIGIO

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Perioperative changes in cardiac biomarkers in juvenile cats during neutering

Keisuke Konishi¹, Mei Sakamoto², Chikara Satake², Mitsuhiro Isaka³*, Seiji Okazaki¹, Shota Kono¹, Takayuki Nakamura¹, Hideki Tashiro¹ and Takahiro Ushigusa¹

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Perioperative myocardial injury (PMI) is commonly caused by myocardial ischemia that develops during or after non-cardiac surgery. It occurs in 17.9% of human patients after non-cardiac surgery due to elevated high-sensitive perioperation cardiac troponin. However, PMI has not been demonstrated in cats. To investigate its occurrence, this study aimed to analyze the perioperative changes in cardiac biomarkers and clinical data, including measurement of vital signs, echocardiography, blood pressure, electrocardiogram, X-ray, and anesthetic profile, in 30 juvenile cats under neutering surgery. All cats had increased high-sensitive cardiac troponin I (hs-clini) postsurgery compared with presurgery. In particular, 48% of cats (14/29) showed elevated hs-cTnl over a reference range after surgery. In all groups, hs-cTnI and systolic arterial blood pressure (SAP) were significantly higher at 0 h and 18 h postoperation than at preoperation. A significant positive correlation was found between hs-cThI and SAP at 18h postoperation. Atrial natriuretic peptides, heart rate, and left ventricular wall thickness were markedly higher at 0 h postoperation than at preoperation; however, respiratory rate and body temperature were significantly lower at 0 h postoperation than at preoperation. Anesthetic time and hs-cTnl were significantly higher at 18 h postoperation in females than in males. Significant positive correlations were observed between hs-cTnl and anesthetic time at 18 h postoperation in females. These results indicate that postoperative hs-cTnl level can greatly increase in juvenile cats and hs-cTnl measurement at perioperation is potentially beneficial for early detection and evaluation of the presence of PMI.

KEYWOKO

atrial natriuretic peptides, high-sensitive cardiac troponin I, juvenile cat, neutering surgery, perioperative myocardial injury

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Superficial digital flexor tendon luxation in a Golden Retriever

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Abstract

Background: Luxation of the superficial digital flexor (SDF) tendon involves the dislocation of the tendon from the groove of the calcaneal tuberosity. Although it is common in Shetland sheepdogs and collies presenting with acute, severe, and non-weight-bearing lameness, it is a rare orthopedic disease in Golden Retrievers.

Case Description: A 13-month-old neutered male Golden Retriever (32.2 kg) with acute right hind lameness and pain, was diagnosed with SDF luxation based on physiological, radiographic, and ultrasound examinations. The surgical procedure used was capsulorrhaphy of the tarsal joint and fixation with Kirschner wire. Postoperatively, the tarsal joint was stretched and externally fixed to prevent tension. The patient showed good gait without pain after pin removal on postoperative day 88.

Conclusion: In clinical practice, the possibility of this condition should be considered in Golden Retrievers presenting with lameness.

Keywords: Golden Retriever, Superficial digital flexor, Surgical procedures, Postoperative complications, Calcaneus.

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Serum concentrations of osteoprotegerin, brain-derived nerve factor, angiotensin II, and endothelin-1 in aging dogs

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Laboratory of Companion Animal Surgery, School of Veterinary Medicine, Rakuno Gakuen University, Hokkaido, Japan

Abstract

Background: Gerontology is a major research topic in veterinary medicine; however, there are few reports on changes in biomarker levels in aged dogs.

Aim: The purpose of this preliminary study was to evaluate the differences in serum biomarker levels between young (less than 36 months) and old (over 108 months) companion dogs.

Methods: We measured the serum concentrations of brain-derived neurotrophic factor (BDNF), osteoprotegerin (OPG), angiotensin II (ANGII), and endothelin-1 (ET-1) in both groups (young: n = 16, 19.8 ± 9.3 months old; old: n = 16, 155.8 ± 22.8 months old).

Results: Although the concentrations of BDNF did not differ between the two groups, the OPG, ANGII, and ET-1 levels were significantly higher in the old companion dogs than in the young dogs (p < 0.05).

Conclusion: OPG, ANGII, and ET-1 concentrations may increase in dogs during aging.

Keywords: Angiotensin II, Brain-derived growth factor, Dogs, Endothelin-1, Osteoprotegerin.

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- 1) Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis.

Itami T, Hanazono K, Makita K, Yamashita K.

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ORIGINAL STUDY



Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis

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This study was presented in part as a poster presentation at the 13th World Congress of Veterinary Anaesthesiology, Venice, Italy, September 2018.

Abstract

Objective: Acidosis decreases myocardial contractile and myofibrillar responsiveness by reducing the calcium sensitivity of contractile proteins, which could reduce the effectiveness of pimobendan. We aimed to assess the cardiovascular effects of pimobendan in dogs subjected to acute respiratory acidosis.

Design: Randomized crossover study with a 2-week washout period.

Setting: University Laboratory.

Animals: Six healthy research Beagle dogs.

Interventions: Anesthetized dogs were administered 2 doses of IV pimobendan during conditions of eucapnia ($Paco_2$ 35–40 mm Hg) and hypercapnia ($Paco_2$ 90–110 mm Hg). Eucapnia was maintained by positive pressure ventilation and hypercapnia was induced by adding exogenous CO_2 to the anesthesia circuit. Heart rate (HR), systemic arterial blood pressure, cardiac output (CO), systemic and pulmonary vascular resistance (SVR and PVR, respectively), and pulmonary arterial pressure (PAP) were measured at baseline and 60 min after administering 0.125 mg/kg (low) and 0.25 mg/kg (high) pimobendan intravenously. Blood gas and biochemical analyses were performed at baseline and at the end of the experiment.

Measurements and Main Results: The median baseline blood pH was 7.41 (range: 7.33-7.45) and 7.03 (range: 6.98-7.09) under conditions of eucapnia and hypercapnia, respectively. The serum concentrations of epinephrine and norepinephrine and the HR, CO, and PAP were higher, and SVR was lower at baseline in hypercapnic dogs. Pimobendan dose-dependently increased CO in eucapnia (baseline: $3.6 \pm 0.2 \text{ L/kg/m}^2$ [mean \pm SE], low: $5.0 \pm 0.4 \text{ L/kg/m}^2$, high: $5.8 \pm 0.5 \text{ L/kg/m}^2$, P < 0.001) and hypercapnia (baseline: $4.9 \pm 0.5 \text{ L/kg/m}^2$, low: $5.8 \pm 0.5 \text{ L/kg/m}^2$, high: $6.2 \pm 0.5 \text{ L/kg/m}^2$, P < 0.001), and increased HR and decreased SVR and PVR under both conditions (P < 0.001). In hypercapnia, the degree of increase or decrease of these cardiovascular measurements (except for PAP) by pimobendan was less than that in the eucapnic dogs.

Abbreviations: cAMP, cyclic adenosine monophosphate; CO, cardiac output; HR, heart rate; MAP, mean arterial pressure; mPAP, mean pulmonary arterial pressure; PDE, phosphodiesterase PAOP, pulmonary artery occlusion pressure: PVR, pulmonary vascular resistance: RAP, right atrial pressure: SVI, stroke volume index: SVR, systemic vascular resistance.

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最終責任者 Takaharu Itami (First Author and Corresponding Author)





Asticle

Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

Kiwamu Hanazono ***, Takaharu Itami ***, Ikuto Hayasaka, Kenjiro Miyoshi, Ai Hori, Keiko Kato and Daiji Endoh **

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Simple Summary: Since there is a lack of information regarding how epoprostenol, a prostacyclin, affects canine renal blood flow (RBF), we investigated the effects of short-term administration of epoprostenol at human doses of 2, 5, and 10 ng/kg/min intravenously for 20 min on RBF in six healthy dogs under anesthesia. The effects of short-term administration were investigated. As the dose of epoprostenol increased, peak systolic and end diastolic velocities of the renal arteries, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase. However, these increases were not significant. These results indicate that the administration of human doses of epoprostenol to dogs does not produce significant changes in renal or systemic circulation.

Abstract: Prostacyclin is an in vivo bioactive substance that regulates renal blood flow (RBF). Information regarding how epoprostenol, a prostacyclin preparation, affects RBF in dogs is lacking. We investigated the effects of short-term epoprostenol administration on RBF in six healthy dogs under anesthesia by administering it intravenously at human doses—2, 5, and 10 ng/kg/min for 20 min. RBF was evaluated before and during epoprostenol administration using pulsed Doppler ultrasonography, and renal perfusion was evaluated using contrast-enhanced ultrasonography. Effects on renal and systemic circulation were evaluated by measuring systolic arterial, mean arterial, diastolic arterial, pulmonary arterial, mean right atrial, and pulmonary capillary wedge pressures; heart rate; and cardiac output. Kruskal—Wallis and Bonferroni multiple comparison tests and Spearman's rank correlation coefficient were used for statistical analyses. As epoprostenol dosage increased, the peak systolic and end diastolic velocity of the renal artery, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase, although not significantly. Our results indicate that human-dose epoprostenol administration in dogs does not cause significant changes in renal or systemic circulation. However, the human doses used may have been too low to produce a clinical effect in dogs.

Keywords: anesthesia; chronic kidney disease; contrast-enhanced ultrasonography; dog; epoprostenol; prostacyclin; pulsed Doppler ultrasonography; renal circulation

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1. Introduction

Chronic kidney disease (CKD) is fatal and causes a persistent and irreversible decline in renal function, which can lead to uremia [1,2]. In patients with CKD, further rapid decline in kidney function can occur, which is termed Acute on Chronic Kidney Disease (ACKD) [3]. Recently, there has been increasing attention on the relationship between CKD progression and interstitial lesions, and it has been reported that interstitial fibrosis, in particular, leads to CKD exacerbation and is closely related to its progression [4,5].

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https://www.mdpi.com/journal/animals

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9103000/pdf/animals-12-01175.pdf

最終責任者 Kiwamu Hanazono & Takaharu Itami (Corresponding Author)

RESEARCH PAPER

Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs

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Abstract

Objective To compare the effects of sevoflurane, propofol and alfaxalone on the neuromuscular blockade induced by a single intravenous bolus of rocuronium in dogs.

Study design A randomized, prospective, crossover experimental study.

Animals A total of eight adult Beagle dogs (four female, four male), weighing 8.9-15.3 kg and aged 5-7 years.

Methods The dogs were anesthetized three times with $1.25\times$ minimum alveolar concentration of sevoflurane (SEVO treatment) and $1.25\times$ minimum infusion rate of propofol (PROP treatment) or alfaxalone (ALFX treatment) at intervals of ≥ 14 days. Neuromuscular function was monitored with train-of-four (TOF) stimulation of the peroneal nerve by acceleromyography. After recording the control TOF ratio (TOFRC), a single bolus dose of rocuronium (1 mg kg $^{-1}$) was administered intravenously. The times from rocuronium administration to achieving TOF count 0 (onset time), from achieving TOF count 0 to the reappearance of TOF count 4 (clinical blockade period), from 25% to 75% of TOFRC (recovery index) and from achieving TOF count 0 to TOF ratio/TOFRC >0.9 (total neuromuscular blockade duration) were recorded.

Results The onset time and recovery index did not differ among the treatments. The median clinical blockade period was longer in the SEVO treatment [27.3 (26.0–30.3) minutes] than in PROP [16.6 (15.4–18.0) minutes; p=0.002] and ALFX [22.4 (18.6–23.1) minutes; p=0.017] treatments; and longer in the ALFX treatment than in the PROP treatment (p=0.020). The mean total neuromuscular blockade duration was longer in the SEVO treatment

 $(43.7 \pm 9.9 \text{ minutes})$ than in PROP $(25.1 \pm 2.7 \text{ minutes}; p < 0.001)$ and ALFX $(32.5 \pm 8.4 \text{ minutes}; p = 0.036)$ treatments.

Conclusions and clinical relevance Compared with alfaxalone and propofol, sevoflurane prolonged rocuroniuminduced neuromuscular blockade by a significantly greater extent in dogs.

Keywords alfaxalone, dogs, neuromuscular blockade, propofol, rocuronium, sevoflurane.

Introduction

Rocuronium bromide, an aminosteroid, is a nondepolarizing neuromuscular blocking agent (NMBA). It has a faster onset as compared with that of vecuronium, but the duration of action is similar between the two (Marshafl et al. 1994; Larijani et al. 1995; Kansanaho et al. 1997). Currently, rocuronium has widespread clinical application in veterinary practice and has been administered to dogs through intravenous (IV) boluses, incremental IV doses or constant rate infusion (CRI) to improve skeletal muscle relaxation during surgical procedures under general anesthesia (Dugdale et al. 2002; Alderson et al. 2007; Auer et al. 2007; Briganti et al. 2015; Haga et al. 2019).

However, administration of NMBAs may lead to a residual block, which is the presence of a neuromuscular blockade during the postoperative period (Jones et al. 2015). Studies in humans have shown that sex, body weight, body temperature, concentration of volatile anesthetic agents and interval between the last NMBA administration and reversal agent administration are associated with a residual block (Vanlinthout et al. 1996; Srivastava & Hunter 2009; Khamtuikrua et al. 2017; Saager et al. 2019).

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The Journal of Veterinary Medical Science



Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits

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ABSTRACT. Recently, a mucosal atomization device (MAO) has been applied in veterinary medicine. In the present study, the maximum volume of nasal atomization without aspiration using MAD was examined in eight healthy female Japanese White (JW) rabbits. Each rabbit had their head and neck examined by computed tomography before and after nasal atomization with four different doses (0.15, 0.3, 0.45, and 0.6 ml per nostril) of diluted contrast medium (1:2 mixture of johexol and saline). This was done under general anesthesia by an intramuscular administration of alfaxalone 2.5 mg/kg, medetomidine 40 µg/kg, and butorphanol 0.4 mg/kg, with a 7-day washout period between each treatment. The diluted contrast medium was distributed in the nasal cavity, external nases, and/or oral cavity in all rabbits receiving each treatment. The intranasal distribution volumes of the contrast medium were 287 (250-333) mm3 (median (interquartile range)) for 0.15 ml, 433 (243-555) mm3 for 0.3 ml, 552 (356-797) mm5 for 0.45 ml, and 529 (356-722) mm3 for 0.6 ml of treatment. The intranasal distribution volume for 0.15 ml treatment tended to be lower than that for 0.6 ml treatment (P=0.083). The contrast medium was deposited in the trachea in one rabbit (12.5%) and four rabbits (50%) receiving treatments of 0.45 and 0.6 ml per nostril, respectively. The maximum volume of nasal atomization without aspiration into the trachea was 0.3 ml per nostril for the JW rabbits.

KEYWORDS: intranasal administration, mucosal atomization device (MAD), nasal atomization volume, rabbit

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9246693/pdf/jvms-84-792.pdf

最終責任者 Ai Hori (Corresponding Author)

The Journal of Veterinary Medical Science



FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC_s/Ao) and the ratio of long to short diameter of the CVC (CVC_c/CVC_c) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (Si), anemia, hypoproteinemia, presence of intraabdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₂/Ao and M8P. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₃/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/ CVC, of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC./Ao of the thorax, CVC_L/CVC_s of the thorax, CVC_s/Ao of the abdomen, and CVC_L/CVC_s of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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出典 doi: 10.1292/jvms.20-0407.

https://www.jstage.jst.go.jp/article/jvms/84/12/84 22-0122/ pdf/-char/en

最終責任者 Kiwamu Hanazono (First Author and Corresponding Author)

Original Article Anesthesiology



Sparing effect of tramadol, lidocaine, dexmedetomidine and their combination on the minimum alveolar concentration of sevoflurane in dogs

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medium, provided the original work is properly cited.

ABSTRACT

Background: Problems associated with using inhalational anaesthesia are numerous in veterinary anaesthesia practice. Decreasing the amount of used inhalational anaesthetic agents and minimising of cardiorespiratory disorders are the standard goals of anaesthetists. Objective: This experimental study was carried out to investigate the sparing effect of intravenous tramadol, lidocaine, dexmedetomidine and their combinations on the minimum alveolar concentration (MAC) of sevoflurane in healthy Beagle dogs.

Methods: This study was conducted on six beagle dogs. Sevoflurane MAC was determined by the tail clamp method on five separate occasions. The dogs received no treatment (control; CONT), tramadol (TRM: 1.5 mg kg¹ intravenously followed by 1.3 mg kg¹ h¹), lidocaine (LID: 2 mg kg¹ intravenously followed by 3 mg kg¹ h²), dexmedetomidine (DEX: 2 μg kg¹ intravenously followed by 2 μg kg¹ h²), and their combination (COMB), respectively. Cardiorespiratory variables were recorded every five minutes and immediately before the application of a noxious stimulus.

Results: The COMB treatment had the greatest sevoflurane MAC-sparing effect (67.4 \pm 13.9%) compared with the other treatments (5.1 \pm 25.3, 12.7 \pm 14.3, and 40.3 \pm 15.1% for TRM, LID, and DEX treatment, respectively). The cardiopulmonary variables remained within the clinically acceptable range following COMB treatment, although the mean arterial pressure was higher and accompanied by bradycardia.

Conclusions: Tramadol-lidocaine-dexmedetomidine co-infusion produced a remarkable sevoflurane MAC-sparing effect in clinically healthy beagle dogs and could result in the alleviation of cardiorespiratory depression caused by sevoflurane. Cardiorespiratory variables should be monitored carefully to avoid undesirable side effects induced by dexmedetomidine.

Keywords: Dog; Tramadol; Lidocaine; Dexmedetomidine; Anaesthesia

獣医解剖学 (Veterinary Anatomy)

Hiromi Ueda

Associate Professor

准教授 植田 弘美

- I. 筆頭または責任著者 <First or Corresponding Author>
- II. その他<Others>
 - 1) Morphological analysis of cell distribution and network structure via gap junctions in swine corneal stroma.

Hoshino M., Takehana K., Hosotani M., Kametani K., Iwasaki T., Hasegawa Y., **<u>Ueda H.</u>**, Watanabe T.

- J. Vet. Med. Sci. 84: 1621-1632. 2022. doi: 10.1292/jvms.22-0329
- 2) Three-dimensional structural analysis of mitochondria composing each subtype of fasttwitch muscle fibers in chicken.

Makita S., KametaniK., Hosotani M., Takahashi N., Iwasaki T., Hasegawa, Y., Takaya T., <u>Ueda H.</u>, Watanabe T.

- J. Vet. Med. Sci. 84: 809-816. 2022. doi: 10.1292/jvms.22-0080
- 3) Comparing chemiluminescent response and intracellular bactericidal activity of bovine blood neutrophils and monocytes against Salmonella Dublin and Escherichia coli. Satoh H., Gondaira S., Higuchi H., <u>Ueda H.</u>, Nohara M., Nagahata H.

Jap. J. Vet. Res. 70: 71-77. 2022. doi: 10.14943/jjvr.70.2.71



FULL PAPER

Anatomy

Morphological analysis of cell distribution and network structure via gap junctions in swine corneal stroma

Nobutaka HOSHINO¹⁾, Kazushige TAKEHANA¹⁾, Marina HOSOTANI¹⁾, Kiyokazu KAMETANI¹⁾, Tomohito IWASAKI²⁾, Yasuhiro HASEGAWA²⁾, Hiromi UEDA¹⁾, Takafumi WATANABE¹⁾*

ABSTRACT. Because of corneal transplantation limitations, there is a need for cornea-specific regenerative medicine. The development of such regenerative medicine has been delayed because of the complex and unique structure of the corneal stroma. Few studies have explored the corneal stroma cell distribution and cell types in vivo. This study investigated regional differences in morphological characteristics and distributions of corneal keratocytes and immunocompetent cells in the corneal stroma to clarify their functions and structural characteristics. The porcine eyeballs were subjected to light microscopy, transmission electron microscopy, scanning electron microscopy, and immunofluorescence staining analyses. Corneal cells were primarily located in the limbus, rather than the center of the cornea; the long keratocyte diameter was largest on the epithelial side of the corneal limbus, while the short diameter was largest on the endothelial side of the central cornea. Moreover, there were significantly more corneal cells on the epithelial side than on the endothelial side in both the central and limbus areas. Gap junctions between cells in the corneal stroma were present on the surfaces of cytoplasmic processes. Many cytoplasmic processes were scattered throughout the corneal stroma; they were connected both vertically and horizontally, forming an intercellular network. Additionally, immunocompetent cells on the epithelial side suggested to participate in this network via gap junctions. The morphology of keratocytes and immunocompetent cells on the epithelial side suggests that they play important roles in corneal homeostasis.

KEYWORDS: corneal keratocytes, corneal stroma, electron microscopy, gap junction, swine

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FULL PAPER

Anatomy

Three-dimensional structural analysis of mitochondria composing each subtype of fast-twitch muscle fibers in chicken

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ABSTRACT. In a previous study, the three-dimensional structures of mitochondria in type I and type IIb muscle fibers of chicken were analyzed. The study reported differences in the shape of the mitochondria and the distribution of lipid droplets. In this study, we three-dimensionally analyzed mitochondria and lipid droplets of type II muscle fiber subtypes IIa, IIb, and IIc of chicken lateral iliotibial muscle in the same field of view using correlative light electron microscopy (CLEM) and array tomography methods. The reconstructed images showed that the mitochondria of type IIa muscle fiber were thick and aligned along the myofibrils, and many lipid droplets were embedded in the mitochondria. The mitochondria of type IIb muscle fibers were intermittent, aligned along the myofibrils, and showed contact between adjacent horizontal mitochondria. No lipid droplets were observed in type IIb muscle fiber. In type IIc muscle fiber, we observed irregularly shaped mitochondria with small diameters aligned along the myofibrils. Lipid droplets not only were embedded in the mitochondria but also existed independently in some cases. The combination of array tomography and CLEM methods enabled three-dimensional electron microscopic observation of mitochondria in different subtypes of type II muscle fibers. The subtypes of type II muscle fibers differed in mitochondrial occupancy and morphology and in lipid droplet distribution, and characteristics that had been demonstrated biochemically were also demonstrated ultrastructurally.

KEYWORDS: array tomography, correlative light electron microscopy, electron microscopy, fast skeletal muscle, mitochondria

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SHORT COMMUNICATION

Experimental Research

Comparing chemiluminescent response and intracellular bactericidal activity of bovine blood neutrophils and monocytes against Salmonella Dublin and Escherichia coli

Hideyasu Satoh¹⁾, Satoshi Gondaira¹⁾, Hidetoshi Higuchi^{1,*)}, Hiromi Ueda²⁾, Masakatsu Nohara³⁾ and Hajime Nagahata^{3,*)}

Received for publication, Mar 7, 2022; accepted, May 15, 2022

Abstract

Chemiluminescent (CL) response and the intracellular killing activity of polymorphonuclear neutrophils (PMNs) and monocytes (MOs) from healthy calves were evaluated to clarify the responsiveness of phagocytes to Salmonella Dublin (S. Dublin) and Escherichia coli (E. coli). CL responses of PMNs and MOs against S. Dublin and E. coli were significantly lower (P < 0.05) than that with opsonized zymosan. The intracellular bactericidal activity of PMNs and MOs was found to be effective against E. coli but not against S. Dublin. These findings indicated that the bactericidal activity of bovine PMNs and MOs against S. Dublin was impaired in innate immune response and that a decreased killing activity against S. Dublin could be a contributing factor for chronic salmonellosis in cattle.

Key Words: bovine monocytes, intracellular bactericidal activity, Salmonella Dublin

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https://eprints.lib.hokudai.ac.jp/journals/item.php?item=104036& handle=2115

86525&jname=117&vname=6811

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食品衛生学 (Food Microbiology and Food Safety)

Masaru Usui

Associate Professor

准教授 臼井 優

- I. 筆頭または責任著者 <First or Corresponding Author>
 - 1) Broad-host-range IncW plasmid harbouring tet(X) in Escherichia coli isolated from pigs in Japan.

Usui M*, Fukuda A, Suzuki Y, Nakajima C, Tamura Y.

J Glob Antimicrob Resist. 22, 97-101. 2022.

DOI: 10.1016/j.jgar.2021.12.012

2) Decreasing the Abundance of Tetracycline-Resistant Escherichia coli in Pig Feces During Nursery Using Flavophospholipol as a Pig Feed Additive Kimura J, Kudo H, Fukuda A, Yamada M, Makita K, Oka K, Takahashi M, Tamura Y, Usui M*.

Vet Anim Sci. 15. 100236. 2022. DOI: 10.1016/j.vas.2022.100236

3) Current Status and Future Perspective of Antimicrobial-Resistant Bacteria and Resistance Genes in Animal-Breeding Environments

Usui M*, Tamura Y, Asai T.

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Broad-host-range IncW plasmid harbouring tet(X) in Escherichia coli isolated from pigs in Japan



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ABSTRACT

Objectives: Tetracyclines are used in veterinary medicine for livestock. Tigecycline, a semisynthetic tetracycline derivative, is a last-resort antimicrobial used to treat multidrug-resistant Gram-negative bacterial infections. The prevalence of variants of the mobile tigecycline resistance gene tet(X) in livestock is increasing worldwide. However, the prevalence of Tet(X) among livestock in Japan is unclear. This study was conducted to clarify the prevalence of Tet(X) in pigs in Japan, focusing on isolation and molecular characterisation of plasmid-mediated tet(X)-positive Escherichia coli through retrospective analysis.

Methods: We retrospectively screened for tigecycline-resistant E. coli strains isolated from pigs. The tigecycline-resistant strain and tet(X)-harbouring plasmid were characterised.

Results: The IncW plasmid harbouring the tet(X) variant [previously named as tet(X6)] was detected in one E. coli isolate from pigs (0.8%; 1/120) in 2012. The tet(X) plasmid was transferable by conjugation to the E. coli ML4909 recipient strain. Some mobile genetic elements (TnAs3 and ISVsa3) were observed in the region surrounding tet(X). The tet(X)-harbouring plasmid shared a conserved backbone with IncW plasmid R388, which is a broad-host-range plasmid.

Conclusion: The emergence and spread of tet(X) variants in Enterobacterales poses a public-health concern. To the best of our knowledge, this is the first report of the emergence of an IncW plasmid harbouring tet(X). Using tetracyclines in livestock exerts selective pressure on the tet(X) plasmid; therefore, prudent use of tetracyclines is required.

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Decreasing the abundance of tetracycline-resistant *Escherichia coli* in pig feces during nursery using flavophospholipol as a pig feed additive

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ABSTRACT

Tetracyclines (TCs) are widely used for livestock, and the high prevalence of TC-resistant Escherichia coli in livestock has become a serious concern worldwide. In Japan, the National Action Plan on Antimicrobial Resistance in 2016 aimed to reduce the TC resistance rate in E. coli derived from livestock. Flavophospholipol (FPL), used as a feed additive, has an inhibitory effect on the spread of plasmid-mediated antimicrobial resistance. The number of TC-resistant E. coli was determined in pigs administered TCs and/or FPL to clarify the effect of FPL on reducing the number of TC-resistant E. coli in pigs. TC-resistant E. coli and their plasmids were then analyzed. The pigs were divided into four groups: control, doxycycline (DOXY; a TC), FPL, and a DOXY-FPL combination. Their feces were collected from the nursing period to the day before being transported to the slaughterhouse, followed by estimation of TC-resistant E. coli (colony-forming units [CFU]/g). The number of TC-resistant E. coli increased with the use of DOXY, suggesting that DOXY administration provides a selective pressure for TC-resistant E. coli. Supplementation with FPL as a feed additive significantly suppressed the increase in the number of TC-resistant E. coli, especially during the DOXY administration period. Transfer and growth inhibition analyses were performed for TC-resistant isolates. FPL inhibited the conjugational transfer and growth of a few TC-resistant E. coli isolates. These results suggest that FPL is effective against the spread of TC-resistant E. coli

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Public Health

Current status and future perspective of antimicrobial-resistant bacteria and resistance genes in animal-breeding environments

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ABSTRACT. The emergence and spread of antimicrobial-resistant bacteria (ARB) and antimicrobial resistance genes (ARGs) are a global public health concern. ARB are transmitted directly or indirectly from animals to humans. The importance of environmental transmission of ARB and ARGs has recently been demonstrated, given the relationships between compost, livestock wastewater, insects, and wildlife. In addition, companion animals and their surrounding environments (veterinary hospitals and homes with companion animals) should be considered owing to their close relationship with humans. This review discusses the current status and future perspectives of ARB and ARGs in animalbreeding environments.

KEYWORDS: animal, antimicrobial resistance, environment, One Health

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∂ ACCESS

Conjugative IncHI2/HI2A plasmids harbouring *mcr-9* in colistinsusceptible *Escherichia coli* isolated from diseased pigs in Japan

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Abstract

Colistin is a last resort antimicrobial used for the treatment of gram-negative bacterial infections. Plasmid-mediated colistin resistance (*mcr*) genes are a cause of global concern, and, thus far, *mcr-1-10* have been identified. In a previous study, we screened *mcr-1-5* in *Escherichia coli* derived from diseased pigs in Japan and reported a high prevalence of *mcr-1, -3* and -5. However, the previous report on the prevalence of *mcr* genes was inaccurate. In the present study, we aimed to clarify the prevalence of all reported variants of *mcr* in *E. coli* derived from the diseased pigs, which were previously screened for *mcr-1-5*. Additionally, we also characterized the *mcr-9*-positive *E. coli*, which was detected in this study. We screened *mcr* in 120 *E. coli* strains from diseased pigs and *mcr-*positive *E. coli* and an *mcr-*carrying plasmid were also characterized. One *mcr-9*-positive colistin-susceptible *E. coli* strain was detected (0.8%). Plasmid-mediated *mcr-9* was transferred to *E. coli* ML4909 as the recipient strain, and it was located on IncHI2/HI2A plasmid p387_L with other antimicrobial resistance genes (ARGs). The region harbouring ARGs including *mcr-9*, was similar to that on the *Klebsiella pneumoniae* chromosome harbouring *mcr-9* isolated in Japan. *mcr-3*, -5 and -9 were detected (4.2%) in colistin-susceptible strains. *mcr-9* was found to be disseminated via the plasmid IncHI2/HI2A p387_L and transferred and inserted into chromosomes via a transposon. Our results suggest that *mcr* genes should be monitored regularly, regardless of their susceptibility to colistin.

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Article

Inactivation of Antibiotic-Resistant Bacteria in Wastewater by Ozone-Based Advanced Water Treatment Processes

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Abstract: The inactivating effect of ozone (O₃)-based advanced oxidation processes (AOPs) (O₃/H₂O₂, O_3/UV , and $O_3/UV/H_2O_2$ systems) on antimicrobial-resistant bacteria (AMRB) and antimicrobialsusceptible bacteria (AMSB) in sewage treatment plant (STP) wastewater was investigated. The AMRB were grouped into six classes: carbapenem-resistant Enterobacteriaceae (CRE), extendedspectrum β -lactamase (ESBL)-producing Enterobacteriaceae (ESBL-E), multidrug-resistant Acinetobacter $(MDRA), \ multidrug\text{-}resistant\ \textit{Pseudomonas\ aeruginosa}\ (MDRP), \ methicillin\text{-}resistant\ \textit{Staphylococcus}$ aureus (MRSA), and vancomycin-resistant Enterococcus (VRE); these classes constituted the World Health Organization (WHO) global priority list of AMRB. The results indicate that O₃-based advanced wastewater treatment inactivated all AMRB and AMSB (>99.9%) after 10 min of treatment, and significant differences (p < 0.5) were not observed in the disinfection of AMRB and AMSB by each treatment. Altered taxonomic diversity of micro-organisms based on 16S rRNA gene sequencing via O_3/UV and $O_3/UV/H_2O_2$ treatment showed that advanced wastewater treatments not only inactivated AMRB but also removed antimicrobial resistance genes (AMRGs) in the wastewater. Consequently, this study recommends the use of advanced wastewater treatments for treating the STP effluent, reducing environmental pollution, and alleviating the potential hazard to human health caused by AMRB, AMSB, and infectious diseases. Overall, this study provides a new method for assessing environmental risks associated with the spread of AMRB and AMSB in aquatic environments, while keeping the water environment safe and maintaining human health.



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Infiltration of hidden antimicrobial resistance among healthy people in a Japanese community

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Background: Under non-antimicrobial selective pressure, antimicrobial-resistant bacteria do not easily become dominant in the microbiota. Furthermore, their low levels prevent detection by isolation, resulting in an underestimation of the prevalence of antimicrobial-resistant bacteria.

 $\textbf{Objectives:} \ \ \text{We evaluated the infiltration of antimicrobial-resistant bacteria and their related } \beta\text{-lactamase genes among healthy people in non-clinical settings.}$

Methods: Cephalosporin- and fluoroquinolone-resistant *Escherichia coli* and *bla* genes were quantified in 217 faecal samples from healthy people in non-clinical settings in Japan. *E. coli* colonies grown on deoxycholate hydrogen sulphide-lactose (DHL) agar, with and without antimicrobials (cefotaxime and ciprofloxacin), were quantified, and *E. coli* isolates were analysed for their susceptibility to antimicrobials and the presence of *bla* genes. DNA extracted from faecal samples was used to quantify *bla* genes using quantitative PCR (qPCR).

Results: The isolation rates of cefotaxime- and ciprofloxacin-resistant *E. coli* were 6.9% and 12.4%, respectively, using agars without antimicrobials, and 12.0% and 24.4%, respectively, using agars with antimicrobials. For samples from which cefotaxime- and ciprofloxacin-resistant *E. coli* were isolated only using agars with antimicrobials, the ratios of cfu on DHL agars with and without antimicrobials were below $-2 \log E$. *coli* harbouring *bla* genes were isolated from 35.0% of the faecal samples using agars, and *bla* genes were detected in 65.0% of faecal DNA samples using qPCR.

Conclusions: Among people carrying cefotaxime- and ciprofloxacin-resistant *E. coli* in non-clinical settings, cefotaxime- and ciprofloxacin-resistant *E. coli* were not dominant in half of the subjects. These individuals may play a role as reservoirs of antimicrobial-resistant bacteria.

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Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

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ABSTRACT Bovine pneumonia is a disease that causes significant economic losses in livestock industries and is vital for animal welfare. The whole-genome sequence of *Pasteurella multocida* strain Pm1, isolated from a calf suffering from pneumonia in Japan, is reported here.

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Distribution and characteristics of carbapenem-resistant and extended-spectrum β -lactamase (ESBL) producing *Escherichia coli* in hospital effluents, sewage treatment plants, and river water in an urban area of Japan



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HIGHLIGHTS

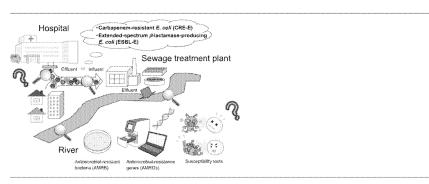
- Occurrence of CRE- and ESBL-E. coli in an urban river basin of Japan was investigated.
- Contributions of AMRB in the hospital effluent to the STP were evaluated.
- STPs were a major source of antimicrobial-resistant bacteria in the river water environment.
- AMRG/16S rRNA gene resistome profiles were similar for river water and wastewa
 ter
- Antimicrobial susceptibility tests showed multidrug resistance in the environment.

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GRAPHICAL ABSTRACT



ABSTRACT

Occurrence of profiles of the carbapenem-resistant *Escherichia coli* (CRE-E) and extended-spectrum β -lactamase (ESBL)producing Escherichia coli (ESBL-E) in an urban river in a sub-catchment of the Yodo River Basin, one of the representative water systems of Japan was investigated. We conducted seasonal and year-round surveys for the antimicrobialresistant bacteria (AMRB) and antimicrobial-resistance genes (AMRGs) in hospital effluents, sewage treatment plant (STP) wastewater, and river water; subsequently, contributions to wastewater discharge into the rivers were estimated by analyses based on the mass flux. Furthermore, the characteristics of AMRB in the water samples were evaluated on the basis of antimicrobial susceptibility tests. CRE-E and ESBL-E were detected in all water samples with mean values 11 and 1900 CFU/mL in the hospital effluent, 58 and 4550 CFU/mL in the STP influent, not detected to 1 CFU/mL in the STP effluent, and 1 and 1 CFU/mL in the STP discharge into the river, respectively. Contributions of the pollution load derived from the STP effluent discharged into the river water were 1 to 21%. The resistome profiles for bla_{IMP} , bla_{TEMs} and bla_{CTX-M} genes in each water sample showed that AMRGs were not completely removed in the wastewater treatment process in the STP, and the relative abundances of bla_{IMP} , bla_{TEM} , and $bla_{\text{CTX-M}}$ genes were almost similar (P<0.05). Susceptibility testing of antimicrobial-resistant E. coli isolates showed that CRE-E and ESBL-E detected in wastewaters and river water were linked to the prevalence of AMRB in clinical settings. These results suggest the importance of conducting environmental risk management of AMRB and AMRGs in the river environment. To our knowledge, this is the first detailed study that links the medical environment to CRE-E and ESBL-E for evaluating

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Colistin Susceptibility in Companion Animal-Derived Escherichia coli, Klebsiella spp., and Enterobacter spp. in Japan: Frequent Isolation of Colistin-Resistant Enterobacter cloacae Complex

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Transmission of colistin-resistant Enterobacterales from companion animals to humans poses a clinical risk as colistin is a last-line antimicrobial agent for treatment of multidrugresistant Gram-negative bacteria including Enterobacterales. In this study, we investigated the colistin susceptibility of 285 Enterobacterales (including 140 Escherichia coli, 86 Klebsiella spp., and 59 Enterobacter spp.) isolated from companion animals in Japan. We further characterized colistin-resistant isolates by multilocus sequence typing (MLST), phylogenetic analysis of hsp60 sequences, and population analysis profiling, to evaluate the potential clinical risk of companion animal-derived colistin-resistant Enterobacterales to humans in line with the One Health approach. All E. coli isolates were susceptible to colistin, and only one Klebsiella spp. isolate (1.2%, 1/86 isolates) was colistin resistant. Enterobacter spp. isolates were frequently colistin resistant (20.3%, 12/59 isolates). In colistin-resistant Enterobacter spp., all except one isolate exhibited colistin heteroresistance by population analysis profiling. These colistin-heteroresistant isolates belonged to clusters I, II, IV, VIII, and XII based on hsp60 phylogeny. MLST analysis revealed that 12 colistin-resistant Enterobacter spp. belonged to the Enterobacter cloacae complex; five Enterobacter kobei (four ST591 and one ST1577), three Enterobacter asburiae (one ST562 and two ST1578), two Enterobacter roggenkampii (ST606 and ST1576), and Enterobacter hormaechei (ST1579) and E. cloacae (ST765) (each one strain). Forty-two percent of the colistin-resistant E. cloacae complex isolates (predominantly ST562 and ST591) belonged to lineages with human clinical isolates. Four E. kobei ST591 isolates were resistant to third-generation cephalosporines, aminoglycosides, and fluroquinolones but remained susceptible to carbapenems.

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最終責任者 Toyotaka SATO (First Author and Corresponding Author)

CASE REPORT Open Access

Chromosomal coharboring of *bla_{IMP-60}* and *mcr-9* in *Enterobacter asburiae* isolated from a Japanese woman with empyema: a case report

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Abstract

Background: Polymyxin E (colistin) is a last-resort antibiotic to treat infections caused by carbapenemase-producing Enterobacteriaceae (CPE). However, reports of CPEs resistant to colistin have been increasing, and the *mcr* genes are emerging as resistance mechanisms. Among them, plasmid-mediate *mcr-9* is known to be associated with colistin resistance, whereas reports on chromosomal *mcr-9* and its association with colistin resistance in humans are few.

Case presentation: We identified *Enterobacter asburiae* harboring mcr-9 and bla_{iMP-60} in the pleural fluid of a patient with empyema. The long-read sequencing technique revealed that these genes were located on its chromosome. Despite the lack of exposure to colistin, the organism showed microcolonies in the inhibition circle in the E-test and disk diffusion test. Antibiotic susceptibility testing by broth microdilution confirmed its resistance to colistin.

Conclusion: Our case report showed that *mcr-9* can be present not only on plasmids but also on the chromosome in *E. asburiae*, and that the presence of *mcr-9* on its chromosome may influence its susceptibility to colistin.

Keywords: mcr-9, Bla_{IMP}, Chromosome, Heteroresistance, Case report

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FULL PAPER

8acteriology

A survey of antimicrobial-resistant Escherichia coli prevalence in wild mammals in Japan using antimicrobial-containing media

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ABSTRACT. The emergence and spread of antimicrobial-resistant bacteria and resistance genes pose serious human and animal health concerns. Therefore, to control antimicrobial-resistant bacteria in the environment, the status of antimicrobial resistance of *Escherichia coli* in a variety of wild mammals and their prevalence were examined using antimicrobial-containing media. In total, 750 isolates were obtained from 274/366 (74.9%) wild mammals, and antimicrobial-resistant *E. coli* was detected in 37/750 isolates (4.9%) from 7 animal species (26/366 [7.1%] individuals). Using antimicrobial-containing media, 14 cefotaxime (CTX)- and 35 nalidixic acid-resistant isolates were obtained from 5 (1.4%) and 17 (4.6%) individuals, respectively. CTX-resistant isolates are obtained from 5 (1.4%) and 17 (4.6%) individuals, respectively. CTX-resistant isolates carried *blaCTX.M.3D blaCTX.M.3D b*

KEYWORDS: antimicrobial resistance, Escherichia coli, human activity, medium, wild mammal

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scientific reports



OPEN

Biological properties of *Staphylococcus* virus ΦSA012 for phage therapy

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Staphylococcus virus ФSA012 has a wide host range and efficient lytic activity. Here, we assessed the biological stability of ФSA012 against temperature, freeze-thawing, and pH to clinically apply the phage. In addition, inoculation of ФSA012 through i.p. and i.v. injections into mice revealed that phages were reached the limit of detection in serum and accumulated notably spleens without inflammation at 48 h post-inoculation. Furthermore, inoculation of ФSA012 through s.c. injections in mice significantly induced IgG, which possesses neutralizing activity against ФSA012 and other Staphylococcus viruses, ФSA039 and ФМR003, but not Pseudomonas viruses ФS12-3 and ФR18 or Escherichia viruses T1, T4, and T7 in vitro. Immunoelectron microscopic analysis showed that purified anti-phage IgG recognizes the long-tail fiber of staphylococcus viruses. Although S. aureus inoculation resulted in a 25% survival rate in a mouse i.p. model, ФSA012 inoculation (i.p.) improved the survival rate to 75%; however, the survival rate of ФSA012-immunized mice decreased to less than non-immunized mice with phage i.v. injection at a MOI of 100. These results indicated that ФSA012 possesses promise for use against staphylococcal infections but we should carefully address the appropriate dose and periods of phage administration. Our findings facilitate understandings of staphylococcus viruses for phage therapy.

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Identification of three novel genes in *Phenuiviridae* detected from *Aedes* mosquitoes in Hokkaido, Japan.

<u>Uchida L</u>, Sakurai Y, Shimooka M, Morales-Vargas RE, Hagiwara K, Muramatsu Y. *Jpn J Infect Dis*. Online ahead of print. 2022. doi: 10.7883/yoken.JJID.2022.179.

II. その他<Others>

Original Article

Identification of Three Novel Genes in *Phenuiviridae* Detected from *Aedes* Mosquitoes in Hokkaido, Japan

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ABSTRACT: Mosquitoes are important arthropod vectors of arboviruses. The family *Phenuiviridae* includes several medically important arboviruses, such as the Rift Valley fever phlebovirus and Toscana phlebovirus. Recent comprehensive genetic analyses have identified many novel mosquito-specific viruses that are phylogenetically related to *Phenuiviridae*. We collected mosquitoes from Hokkaido in northern Japan, and conducted reverse transcription polymerase chain reactions (RT-PCRs) targeting the RNA-dependent RNA polymerase (*RdRp*) gene of *Phenuiviridae*. A total of 285 pools, comprising 3,082 mosquitoes from 2 genera and 8 species, were collected. Partial *RdRp* sequences were detected in 97 pools, which allowed us to classify the viruses into 3 clusters provisionally designated as Etutanne virus (ETTV) 1, 2, and 3. The virus most closely related to ETTVs is Narangue virus (family *Phenuiviridae*, genus *Mobuvirus*), which was detected in *Mansonia* mosquitoes; the nucleotide and amino acid sequences of the Narangue virus are 58.4–66.2% and 64.7–86.7% similar, respectively, to those of ETTVs. PCR and RT-PCR using DNA and RNase digestion methods showed that the ETTVs are RNA viruses that do not form non-retroviral integrated RNA virus sequences in the mosquito genome.

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- I. 筆頭または責任著者 <First or Corresponding Author>
 - 1) Visualising the hepatic vascular architecture using superb microvascular imaging in a dog with severe hepatic fibrosis.

Tamura M, Ohta H.

J. Small Anim. Pract. 63(9):717. 2022. doi: 10.1111/jsap.13521.

II. その他<Others>

- Local cerebral blood flow assessment using transcranial doppler ultrasonography in a dog with brain infarction in the right middle cerebral artery territory.
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- 2) Exploration of serum biomarkers in dogs with malignant melanoma receiving anti-PD-L1 therapy and potential of COX-2 inhibition for combination therapy. Maekawa N, Konnai S, Asano Y, Sajiki Y, Deguchi T, Okagawa T, Watari K, Takeuchi H, Takagi S, Hosoya K, Kim S, Ohta H, Kato Y, Suzuki Y, Murata S, Ohashi K. *Scientific reports* 12(1):9265-9265. 2022. doi: 10.1038/s41598-022-13484-8.
- 3) Characterization of mucin gene expression and goblet cell proportion in inflammatory colorectal polyps in miniature dachshunds.

Nagata N, <u>Ohta H</u>, Yokoyama N, Teoh YB, Sasaki N, Nakamura K, Takiguchi M. *J. Vet. Med. Sci.* 84(6):872-876. 2022. doi: 0.1292/jvms.22-0076.

- 4) Transcranial Doppler ultrasonography detects the elevation of cerebral blood flow during ictal-phase of pentetrazol-induced seizures in dogs.

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Front. Vet. Sci. 7;9:854042. 2022. doi: 10.3389/fvets.2022.854042.

IMAGES IN SMALL ANIMAL PRACTICE

Visualising the hepatic vascular architecture using superb microvascular imaging in a dog with severe hepatic fibrosis

Superb microvascular imaging (SMI) is a novel Doppler ultrasound imaging technology using a new clutter suppression algorithm to identify and eliminate tissue movement, extract blood flow signals at a relatively high frame rate, and provide high-resolution details of vascular branches without an ultrasound contrast medium. Monochrome SMI was performed to evaluate the hepatic vascular architecture in a 9-month-old Pomeranian dog with histopathological hepatic fibrosis (Fig. 1A) using an ultrasound (Aplio" 500; Canon Medical Systems, Tochigi, Japan) and a 10-MHz linear probe (PLT-1005BT: Canon Medical Systems Corporation). The monochrome SMI was set with a low speed of 0.9 to 2.6 cm/s and a frame rate of 50 to 600%. The dog was anaesthetised and placed in a left lateral recumbent position. The hepatic parenchyma at the level of the porta hepatic was scanned in a transverse section. via the intercostal approach. Monochrome SMI revealed poor ramification and tapering of the main branch of the hepatic vessels (Fig. 1B). Smart three-dimensional SMI (3D-SMI), a volumerendering technology, was used to fully observe the 3D pattern. visualisation of the vascular architectures. In the smart 3D-SMI mode, the transducer moves at a uniform and constant speed, and

a 3D vascular image can be reconstructed from a monochrome SM image. We also performed smart 3D-SMI in a 3-year-old healthy anaesthetised beagle dog for comparison (Supporting Information Material S1). Smart 3D-SMI detected severe torthosity of the main branches and unevenness of branching in the affected dog (Fig 1C) compared with the healthy dog (Fig 1D). These remarkable vascular changes were likely caused by excessive accumulation of the estracellular matrix in the hepatic parenchyma and the pressure of growth and expansion of regenerative nodules.

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HOTE

Internal Medicine

Local cerebral blood flow assessment using transcranial Doppler ultrasonography in a dog with brain infarction in the right middle cerebral artery territory

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ABSTRACE. A 12-year-old neutered male Chihuahua was diagnosed with acute brain infarction in the right middle cerebral artery (MCA) territory. Transcranial Doppler ultrasonography (TCD) was performed to assess the local cerebral blood flow at the time of diagnosis and after 4 and 31 hr. Initially, the right MCA retained blood flow but with a lower cerebral blood flow velocity (CBFV; 14.9 cm/sec) than the left MCA (27.9 cm/sec). The TCD vascular resistance variables were higher in the right than in the left MCA. An increase in the CBFV and a decrease in TCD vascular resistance variables were observed, consistent with improvements in neurological symptoms. TCD can be a non-invasive, and easy-to-use modality for bedside monitoring of cerebral edema and infarction.

KEYWORDS: critical care, ischemic brain disease, neuroimaging, neurology, ultrasonography

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scientific reports

and the same

OPEN Exploration of serum biomarkers in dogs with malignant melanoma receiving anti-PD-L1 therapy and potential of COX-2 inhibition for combination therapy

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immune checkpoint inhibitors (ICIs) such as anti-PD-L1 antibodies are widely used to treat human cancers, and growing evidence suggests that ICIs are promising treatments for canine malignancies. However, only some canine oral malignant melanoma (OMM) cases respond to Kis. To explore biomarkers predictive of survival in dogs with pulmonary metastatic OMM receiving the anti-PD-L1 antibody c4G12 (n = 27), serum concentrations of prostaglandin E2 (PGE₂), cytokines, chemokines, and growth factors were measured prior to treatment initiation. Among 12 factors tested, PGE₃, interleukin (IL)-12p40, IL-8, monocyte chemotectic protein-1 (MCP-1), and stem cell factor (SCF) were higher in OMM dogs compared to healthy dogs (n=8). Further, lower baseline serum PGE., MCP-1, and varcular endothelial growth factor (VEGF)-A concentrations as well as higher IL-2, IL-12, and SCF concentrations predicted prolonged overall survival. These observations suggest that PGE, confers resistance against anti-PD-L1 therapy through immunosuppression and thus is a candidate target for combination therapy. Indeed, PGE, suppressed IL-2 and interferon (IFN)-y production by stimulated canine peripheral blood mononuclear cells (PBMCs), while inhibition of PGE; biosynthesis using the COX-2 inhibitor meloxicum in combination with c4G12 enhanced Th1 cytokine production by PBMCs. Thus, serum PGE, may be predictive of c4G12 treatment response, and concomitant use of CCX-2 inhibitors may enhance ICI antitumor efficacy.

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NOTE

Internal Medicine

Characterization of mucin gene expression and goblet cell proportion in inflammatory colorectal polyps in miniature dachshunds

Noriyuki NAGATA¹⁾, Hiroshi OHTA²⁾, Nozomu YOKOYAMA¹⁾, Yong Bin TEOH³⁾, Noboru SASAKI³⁾, Kensuke NAKAMURA³⁾ and Mitsuyoshi TAKIGUCHI³⁾*

J. Vet. Med. Sci. 84(6): 872–876, 2022 doi: 10.1292/jvms.22-0076

Received: 22 February 2022 Accepted: 25 April 2022 Advanced Epub: 5 May 2022 ABSTRACT. Hyperplastic goblet cells and abundant mucus are significant characteristics of inflammatory colorectal polyps (ICRPs) in miniature dachshunds. In this study, selected mucin gene expressions and goblet cell proportions were evaluated in miniature dachshunds with ICRPs and in healthy dogs. *Mucin 2 (MUC2)* gene expression was not significantly different among the groups, whereas *mucin 5AC (MUC5AC)* gene expression was significantly higher in the polypoid lesions than in healthy colonic mucosa. Although the percentage of goblet cells in the upper crypt regions did not significantly differ between the groups, that in the lower crypt regions was significantly decreased in polypoid lesions. In conclusion, increased *MUC5AC* gene expression and goblet cell proportion changes may be associated with the pathogenesis of ICRPs.

KEYWORDS: canine, goblet cell, inflammatory colorectal polyp, mucin

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AJVR



Transcranial Doppler ultrasonography detects the elevation of cerebral blood flow during ictal-phase of pentetrazol-induced seizures in dogs

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OBJECTIVE

To investigate the association between changes in cerebral blood flow and electrographic epileptic seizure in dogs using transcranial Doppler ultrasonography (TCD).

ANIMALS

6 healthy Beagle dogs.

PROCEDURES

Each dog was administered pentetrazol (1.5 mg/kg/min) or saline (0.9% NaCl) solution under general anesthesia with continuous infusion of propofol. Both pentetrazol and saline solution were administered to all 6 dogs, with at least 26 days interval between the experiments. Blood flow waveforms in the middle cerebral artery and the basilar artery were obtained using TCD at baseline, after pentetrazol administration, and after diazepam administration. TCD velocities, including peak systolic velocity, end-diastolic velocity, and mean velocity and resistance variables, were determined from the Doppler waveforms.

RESULTS

During ictal-phase of pentetrazol-induced seizures, the TCD velocities significantly increased in the basilar and middle cerebral arteries while TCD vascular resistance variables did not change in either artery. The TCD velocities significantly decreased after diazepam administration. Systemic parameters, such as the heart rate, mean arterial pressure, systemic vascular resistance, cardiac index, end-tidal carbon dioxide, oxygen saturation, and body temperature, did not change significantly during seizures.

CLINICAL RELEVANCE

This study showed that cerebral blood flow, as obtained from TCD velocities, increased by 130% during ictal-phase of pentetrazol-induced seizures in dogs. The elevated velocities returned to baseline after seizure suppression. Thus, TCD may be used to detect electrographic seizures during the treatment of status epilepticus in dogs, and further clinical studies clarifying the association between changes in cerebral blood flow and non-convulsive seizure cases are needed.

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Case Report: Usefulness of Drip Infusion Cholangiography With Computed Tomography for the Diagnosis of Biloma in a Dog

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Bliomas are encapsulated collections of bile outside or inside the billary tract within the abdominal cavity. For diagnostic and therapeutic approaches, it is important to identify the origin of bile leaks from the billary tract. This case report describes the usefulness of drip infusion cholangiography with computed fornography (DIC-CT) for detecting the site of bile leakage in a dog with biloma. A 10-year-old, castrated male Pomeranian dog was referred to our department for gastrointestinal signs. Abdominal ultrasonography detected galloladder mucoceie without evidence of defect on the wall and well-defined anechoic localized fluid accumulation around the right division of the liver. On the other hand, there was only a small amount of ascites in the abdominal cavity. The accumulated fluid collected through abdominocentesis had a billrubin concentration of 11.4 mg/di, which was more than twice as high as that in serum (0.4 mg/df), but had absence of pyogenic bacteria. The DIC-CT with megiumine lotroxate showed two well-defined large. fluid collections; one between right medial and lateral lobe and the other between the right lateral lobe and caudate process of caudate lobe. Three-dimensional DIC-CT views that the former was enhanced by the contrast agent and that it communicated with an intrahepatic bile duct of the right lateral lobe. Moreover, the DIC-CT images confirmed communication with each fluid collections. After 6 days of hospitalization, a decrease in the amount of accumulated fluid was confirmed, after which cholecystectomy was performed. The dog was discharged from the hospital without complications. No signs of bile leakage were observed on follow-up imaging on postoperative day 10. According to authors knowledge, this has been the first report to show that DIC-CT can be useful for determining the origin of bile leakage in dogs with bilomas.

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 - 1) Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs.
 - Chen IY, Tamogi H, Wei Y, Kato K, Itami T, <u>Sano T</u>, Yamashita K. *Vet Anaesth Analg.* 49:36-44. 2022. doi: 10.1016/j.vaa.2021.10.002.
 - 2) Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits.
 - Wei Y, Hori A, Chen IY, Tamogi H, Hirokawa T, Kato K, Itami T, <u>Sano T</u>, Yamashita K.
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RESEARCH PAPER

Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs

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Abstract

Objective To compare the effects of sevoflurane, propofol and alfaxalone on the neuromuscular blockade induced by a single intravenous bolus of rocuronium in dogs.

Study design A randomized, prospective, crossover experimental study.

Animals A total of eight adult Beagle dogs (four female, four male), weighing 8.9-15.3 kg and aged 5-7 years.

Methods The dogs were anesthetized three times with $1.25\times$ minimum alveolar concentration of sevoflurane (SEVO treatment) and $1.25\times$ minimum infusion rate of propofol (PROP treatment) or alfaxalone (ALFX treatment) at intervals of ≥14 days. Neuromuscular function was monitored with train-of-four (TOF) stimulation of the peroneal nerve by acceleromyography. After recording the control TOF ratio (TOFRC), a single bolus dose of rocuronium (1 mg kg $^{-1}$) was administered intravenously. The times from rocuronium administration to achieving TOF count 0 (onset time), from achieving TOF count 0 to the reappearance of TOF count 4 (clinical blockade period), from 25% to 75% of TOFRC (recovery index) and from achieving TOF count 0 to TOF ratio/TOFRC >0.9 (total neuromuscular blockade duration) were recorded.

Results The onset time and recovery index did not differ among the treatments. The median clinical blockade period was longer in the SEVO treatment [27.3 (26.0–30.3) minutes] than in PROP [16.6 (15.4–18.0) minutes; p=0.002] and ALFX [22.4 (18.6–23.1) minutes; p=0.017] treatments; and longer in the ALFX treatment than in the PROP treatment (p=0.020). The mean total neuromuscular blockade duration was longer in the SEVO treatment

 $(43.7 \pm 9.9 \text{ minutes})$ than in PROP $(25.1 \pm 2.7 \text{ minutes}; p < 0.001)$ and ALFX $(32.5 \pm 8.4 \text{ minutes}; p = 0.036)$ treatments.

Conclusions and clinical relevance Compared with alfaxalone and propofol, sevoflurane prolonged rocuroniuminduced neuromuscular blockade by a significantly greater extent in dogs.

Keywords alfaxalone, dogs, neuromuscular blockade, propofol, rocuronium, sevoflurane.

Introduction

Rocuronium bromide, an aminosteroid, is a nondepolarizing neuromuscular blocking agent (NMBA). It has a faster onset as compared with that of vecuronium, but the duration of action is similar between the two (Marshall et al. 1994: Larijani et al. 1995; Kansanaho et al. 1997). Currently, rocuronium has widespread clinical application in veterinary practice and has been administered to dogs through intravenous (IV) boluses, incremental IV doses or constant rate infusion (CRI) to improve skeletal muscle relaxation during surgical procedures under general anesthesia (Dugdale et al. 2002; Alderson et al. 2007; Auer et al. 2007; Briganti et al. 2015; Haga et al. 2019). However, administration of NMBAs may lead to a residual block, which is the presence of a neuromuscular blockade during the postoperative period (Jones et al. 2015). Studies in humans have shown that sex, body weight, body temperature, concentration of volatile anesthetic agents and interval between the last NMBA administration and reversal agent administration are associated with a residual block (Vanlinthout et al. 1996; Srivastava & Hunter 2009; Khamtuíkrua et al. 2017; Saager et al. 2019).

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The Journal of Veterinary Medical



Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits

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ABSTRACT. Recently, a mucosal atomization device (MAD) has been applied in veterinary medicine. In the present study, the maximum volume of nasal atomization without aspiration using MAD was examined in eight healthy female Japanese White (JW) rabbits. Each rabbit had their head and neck examined by computed tomography before and after nasal atomization with four different doses (0.15, 0.3, 0.45, and 0.6 ml per nostril) of diluted contrast medium (1:2 mixture of lohexol and saline). This was done under general anesthesia by an intramuscular administration of alfaxalone 2.5 mg/kg, medetomidine 40 µg/kg, and butorphanol 0.4 mg/kg, with a 7-day washout period between each treatment. The diluted contrast medium was distributed in the nasal cavity, external nares, and/or oral cavity in all rabbits receiving each treatment. The intranasal distribution volumes of the contrast medium were 287 (250–333) mm³ (median (interquartile range)) for 0.15 ml, 433 (243-555) mm3 for 0.3 ml, 552 (356-797) mm3 for 0.45 ml, and 529 (356-722) mm³ for 0.6 ml of treatment. The intranasal distribution volume for 0.15 ml treatment tended to be lower than that for 0.6 ml treatment (P=0.083). The contrast medium was deposited in the trachea in one rabbit (12.5%) and four rabbits (50%) receiving treatments of 0.45 and 0.6 ml per nostril, respectively. The maximum volume of nasal atomization without aspiration into the trachea was 0.3 ml per nostril for the JW rabbits.

KEYWORDS: Intranasal administration, mucosal atomization device (MAD), nasal atomization volume, rabbit

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最終責任者 Ai Hori (Corresponding Author)

The Journal of Veterinary Medical Science



FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

Kiwamu HANAZONO^{1)*}, Mako NAKAMOTO¹⁾, Ai HORI¹⁾, Kenjiro MIYOSHI¹⁾, Tetsuya NAKADE¹⁾, Takaharu ITAMI¹⁾, Tadashi SANO¹⁾, Keiko KATO¹⁾, Akifumi ITO¹⁾, Kakeru TANAKA¹⁾, Kazuto YAMASHITA¹⁾, Daiji ENDOH¹⁾

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC₃/Ao) and the ratio of long to short diameter of the CVC (CVC₄/CVC₅) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₃/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₃/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC₃/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₄/CVC₅ of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₃/Ao of the thorax, CVC₄/Ao of the abdomen, and CVC₄/CVC₅ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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最終責任者 Kiwamu Hanazono (First Author and Corresponding Author)

Original Article Anesthesiology



Sparing effect of tramadol, lidocaine, dexmedetomidine and their combination on the minimum alveolar concentration of sevoflurane in dogs

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medium, provided the original work is properly cited.

ABSTRACT

Background: Problems associated with using inhalational anaesthesia are numerous in veterinary anaesthesia practice. Decreasing the amount of used inhalational anaesthetic agents and minimising of cardiorespiratory disorders are the standard goals of anaesthetists. Objective: This experimental study was carried out to investigate the sparing effect of intravenous tramadol, lidocaine, dexmedetomidine and their combinations on the minimum alveolar concentration (MAC) of sevoflurane in healthy Beagle dogs.

Methods: This study was conducted on six beagle dogs. Sevoflurane MAC was determined by the tail clamp method on five separate occasions. The dogs received no treatment (control; CONT), tramadol (TRM: 1.5 mg kg¹ intravenously followed by 1.3 mg kg¹ h²), lidocaine (LID: 2 mg kg¹ intravenously followed by 3 mg kg¹ h¹), dexmedetomidine (DEX: 2 $\mu g \ kg¹$ intravenously followed by 2 $\mu g \ kg¹$ h²), and their combination (COMB), respectively. Cardiorespiratory variables were recorded every five minutes and immediately before the application of a noxious stimulus.

Results: The COMB treatment had the greatest sevoflurane MAC-sparing effect (67.4 \pm 13.9%) compared with the other treatments (5.1 \pm 25.3, 12.7 \pm 14.3, and 40.3 \pm 15.1% for TRM, LID, and DEX treatment, respectively). The cardiopulmonary variables remained within the clinically acceptable range following COMB treatment, although the mean arterial pressure was higher and accompanied by bradycardia.

Conclusions: Tramadol-lidocaine-dexmedetomidine co-infusion produced a remarkable sevoflurane MAC-sparing effect in clinically healthy beagle dogs and could result in the alleviation of cardiorespiratory depression caused by sevoflurane. Cardiorespiratory variables should be monitored carefully to avoid undesirable side effects induced by dexmedetomidine.

Keywords: Dog; Tramadol; Lidocaine; Dexmedetomidine; Anaesthesia

獣医臨床病理学 (Veterinary Clinicopathology)

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Identification and phylogenetic analysis of *Babesia* parasites in domestic dogs in Nigeria,

<u>Hirata H</u>, Omobowale T, Adebayo O, Asanuma N, Haraguchi A, Murakami Y, Kusakisako K, Ikeda K, Asakawa M, Suzuki K, Ishihara C and Ikadai H. *J. Vet. Med. Sci.* 84(3): 338-341. 2022. doi: 10.1292/jvms.21-0636.

Ⅱ. その他<Others>

1) Endotoxin activity and leukocytic STAT3 mRNA alterations differ according to age in lipopolysaccharide-challenged calves.

Nishi Y., Murakami Y., Teshima S., Tsukano K., Otsuka M., <u>Hirata H.</u>, Tsuchiya M., Suzuki K.

Res Vet Sci. 152: 300-306. 2022. doi: 10.1016/j.rvsc.2022.08.028.

2) Comparison of the alkalizing abilities between 1.35% sodium bicarbonate solutions with and without dextrose in healthy calves.

Sato K., Tsukano K., Kurata M., Ajito T., <u>Hirata H.</u>, Suzuki K. *J. Vet. Med. Sci.* 84(10): 1335-1339. 2022. doi: 10.1292/jvms.22-0289.

3) Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs.

Murakami Y., Tsukano K., Hirata H., Koie H., Suzuki K.

Thai J Vet Med. 52(2): 369-372. 2022. doi.org/10.14456/tjvm.2022.41



NOTE

Parasitology

Identification and phylogenetic analysis of *Babesia* parasites in domestic dogs in Nigeria

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ABSTRACT. The present study examined the presence of *Babesia* parasites in 104 domestic dogs in Nigeria. Sequentially, *Babesia* parasites infecting domestic dogs underwent genetic and phylogenetic analyses. The results of nested PCR based on the Piroplasmida 185 rRNA gene illustrated that 13.5% (14/104) of the samples were positive. The obtained positive samples determined the nucleotide sequences of the 185 rRNA genes. In the genetic and phylogenetic analyses, four of five nucleotide sequences were similar to *Babesia canis rossi*, and one sample exhibited a close similarity to a *Babesia* sp. isolated from a raccoon in Hokkaido, Japan. The present study revealed the widespread presence of *B. canis rossi* among domestic dogs in Nigeria.

KEY WORDS: 18S rRNA, Babesia canis, domestic dog, Nigeria, phylogenetic analysis

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Endotoxin activity and leukocytic STAT3 mRNA alterations differ according to age in lipopolysaccharide-challenged calves

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ARTICLE INFO

Kevwords: Acute phase response Calf Endotoxin STAT3

ABSTRACT

The objective of this study was to investigate the age difference in the response to endotoxin in calves related to the plasma endotoxin activity and mRNA expression of cytokines. Fifteen calves were divided into three groups: control (191 \pm 21 days), weaning (162.4 \pm 17.5 days), and calf (22.4 \pm 8.2 days). The weaning and calf groups received 2.5 µg/kg of ultrapure O111:B4 LPS in 10 mL of each autologous serum, whereas the control calves received a similar volume of saline. Blood samples were collected at 0, 0.5, 1, 2, 4, 8, 12, and 24 h. Liver samples were collected by ultrasound-guided liver biopsy at 0, 2, 4, and 24 h. Plasma endotoxin activity was measured by the limulus amebocyte lysate kinetic turbidimetric assay. The mRNA expression level of GAPDH, TLR-4, NF-xB2, TNF- α , IL-6, and STAT3 in leukocytes and the liver was measured by real-time PCR.

Following LPS challenge, the maximal plasma endotoxin activity, and leukocytic expression of TLR4, NF- κ B2, TNF- α , and STAT3 were reached at 0.5, 4, 2-4, 2-4, and 4 h, respectively, in weaning and calf groups. The endotoxin activity in calf remained high until 2 h. Furthermore, the expression of leukocytic STAT3 mRNA in calf was not significantly different from the pre-value. In contrast, STAT3 mRNA in weaning markedly increased at 2 and 4 h. Therefore, this study provides new information to the literature of immune and inflammatory responses in calves.

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FULL PAPER

Internal Medicine

Comparison of the alkalizing abilities between 1.35% sodium bicarbonate solutions with and without dextrose in healthy calves

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ABSTRACT. The present study aimed to clarify the alkalizing ability of 1.35% isotonic sodium bicarbonate solution (ISBS), which did not contain dextrose, compared with that of 1.35% isotonic bicarbonate sodium solution containing 4.03% dextrose (ISBD) in healthy calves. The calves were intravenously administered with 20.7 mL/kg of the solutions for 30 min as the volume required to correct base deficit of 10 mM. ISBS increased the blood pH, HCO $_3^-$, and base excess from 7.44 \pm 0.02, 29.6 \pm 1.9 mM, and 5.3 \pm 2.1 mM to 7.49 \pm 0.02, 36.9 \pm 2.3 mM, and 13.5 \pm 2.6 mM respectively (P<0.05). These factors for the ISBD group increased from 7.41 \pm 0.02, 29.0 \pm 1.1 mM, and 4.5 \pm 1.3 mM to 7.43 \pm 0.02, 33.5 \pm 1.9 mM, and 9.5 \pm 1.7 mM (P<0.05), respectively. Furthermore, in the ISBD group, the relative plasma volume and blood glucose level increased while the K* level decreased, which did not occur in the ISBS group. Therefore, the results revealed that ISBS had better alkalizing ability in calves than ISBD.

KEYWORDS: calf, dextrose, hyperkalemia, isotonic sodium bicarbonate, metabolic acidosis

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Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs

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Hiroshi KOIE² Kazuyuki SUZUKI¹

Abstract

This study aimed to investigate, using magnetic resonance imaging, whether continuous hypertonic saline (HSS) infusion induces a superior vasodilating effect on the encephalic vessels compared to bolus infusion in dogs. The relative cross-sectional area of superior sagittal sinus increased to 1.96 ± 0.09 and 1.69 ± 0.31 times of the pre-value in the continuous and bolus groups, respectively, at t=30 min (p<0.001). However, the relative cross-sectional area of superior sagittal sinus was larger in the continuous group than that in the bolus group (p<0.001). The results suggest that continuous infusion of HSS might be superior to bolus infusion in inducing vasodilatation of the encephalic circulation.

Keywords: encephalic circulation, fluid therapy, hypertonic saline, magnetic resonance imaging, superior sagittal sinus
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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Sodium butyrate administration modulates the ruminal villus height, inflammationrelated gene expression, and plasma hormones concentration in dry cows fed a highfiber diet.

<u>Fukumori R</u>, Doi Y, Mochizuki T, Oikawa S, Gondaira S, Iwasaki T, Izumi K. *Animal Science Journal* 93: e13791. 2022. doi: 10.1111/asj.13791.

2) Effects of digestive drug containing betaine hydrochloride on dry matter intake, rumen profiles, and blood concentrations of gut hormones in non-lactating cows.

Fukumori R, Takayama Y, Izumi K, Oikawa S.

The Japanese Journal of Animal Hygiene 47:197-204.2022.

II. その他<Others>

RESEARCH ARTICLE



Sodium butyrate administration modulates the ruminal villus height, inflammation-related gene expression, and plasma hormones concentration in dry cows fed a high-fiber diet

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Funding information

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Abstract

The objectives of this study were to evaluate the effects of sodium butyrate on the ruminal villus morphology, mRNA expression associated with nutrient metabolism and inflammation in the ruminal epithelium, and plasma concentrations of metabolites and hormones in non-lactating cows fed a high-fiber diet. Four Holstein cows with a rumen cannula were assigned to two treatments in a crossover design. The treatments were ruminal administration of sodium butyrate premix or control premix before feeding to cows fed the same total mixed ration mainly composed of glass silage once a day. Sodium butyrate was provided at a butyrate dose of 0.04% per kg body weight. The control premix was made by replacing sodium-butyrate with wheat bran. The plasma β-hydroxybutyrate concentration increased 3 to 6 h after the butyrate premix administration but returned to a concentration similar to that of the control before feeding. After continuous administration, increases in the ruminal villus height and plasma concentration of glucagon-like peptide-2, and lower gene expression of TNF-α, IL-1β, and TLR-2 in the rumen epithelium were observed in cows supplied with the butyrate premix. These results showed that sodium butyrate affects rumen epithelial morphology and plasma concentrations of hormones even under a low fermentable diet.

KEYWORDS

butyrate, dairy cow, GLP-2, inflammation-related gene, rumen papillae

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Original report

Effects of digestive drug containing betaine hydrochloride on dry matter intake, rumen profiles, and blood concentrations of gut hormones in non-lactating cows

Rika Fukumori 1, Yumiko Takayama 1, Ken-ichi Izumi 2, Shin Oikawa 1, **

塩酸ベタイン含有消化器改善薬の投与が牛の乾物摂取量, ルーメン性状および血中消化管ホルモン濃度に及ぼす影響

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> * Author for Correspondence; Shin Oikawa (oishin@rakuno.ac.jp)) (Received 9. Jun. 2021 / Accepted 29. Nov. 2021)

Summary

The objective of this study was to investigate the effects of digestive drug containing betaine hydrochloride (BH) administration on dry matter intake, the rumen and blood properties in cattle. Four non-lactating cows, each fitted with a rumen cannula, were randomly assigned to 2 treatments in a crossover design. The 2 experimental periods were each 7-d long, with a 3-d washout period separating them. The treatments were oral administration of BH or water (WT). Oral administration was conducted once a day just before feeding. BH was provided as Bio-Pair (TOA Biopharma, CO. Ltd., Tokyo, Japan) at the dose of 90 g/d/cow. Ruminal fluid and blood samples were collected on d 7 over time relative to feeding for determining plasma concentrations of gut hormones (insulin, glucagon like peptide-2 [GLP-2], and ghrelin) and metabolites (glucose, urea-nitrogen, and total-cholesterol) and ruminal concentrations of volatile fatty acids. Dry matter intake was determined from d 5 to 7 of each period for each cow. Ruminal pH was recorded every 15 min through the sample collection period. The pH was not affected by BH administration, but the ruminal propionate proportion was lower and the acetate proportion tended to be higher for cows in the BH group than for cows in the WT group. BH administration decreased the plasma concentrations of glucose and total cholesterol, and increased those of insulin and GLP-2. Regarding ghrelin, an orexigenic hormone, no effect of BH administration was observed, and dry matter intake was not different between the treatments. The above findings indicated that BH did not affect feed intake, but it might affect rumen VFA and blood properties, causing metabolic shifts to anabolism at this dosage of BH.

Key words: betaine hydrochloride, gut peptides, feed intake, metabolism

_______ Jpn. J. Anim. Hyg. 47, 197~204 (2022)

最終責任者 Shin Oikawa (Corresponding Author)

獣医生理学(Veterinary Physiology)

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- I. 筆頭または責任著者 <First or Corresponding Author>
- Ⅱ. その他<Others>
 - 1) Intravenous administration of xenin-25 accelerates cyclic ruminal contractions in healthy conscious sheep.

Onaga T, Sakai A, Yasui Y.

Neuropeptides 96:102293. 2022. doi: 10.1016/j.npep. 2022.114073.

2) Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep.

Onaga T, Yasui Y, Hayashi H.

Gen Comp Endocrinol. 326:114073. 2022. doi: 10.1016/j.ygcen. 2022. 114073.



Neuropeptides



journal homepage: www.elsavier.com/locate/npep



Intravenous administration of xenin-25 accelerates cyclic ruminal contractions in healthy conscious sheep

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ARTICLE INFO

Krywords: Sheep Forestomach Rumen contractions Xenopsin-related peptides

ABSTRACT

The present study aimed to determine the effect and mode of action of the intravenous injection of xenin-25 on cyclic contractions of the rumen in healthy conscious sheep and mode of its action. Clinically healthy male sheep were equipped with a rumen cannula by surgery under anesthesia, and ruminal contractions were recorded with manometry in conscious animals after the recovery period. Intravenous xenin-25 injection induced a cluster of premature ruminal phasic contractions in a dose-dependent manner between 0.03 and 1 nmol/kg, and the change at the highest dose was statistically significant. In contrast, intravenous neurotensin injection inhibited the amplitude of cyclic rumen contractions. The xenin-25 effect was not significantly altered by prior injection of the neurotensin receptor subtype-1 antagonist SR 48692 at 30 and 100 nmol/kg. After euthanasia the ruminal muscles were excised for in vitro experiments. A single xenin-25 application (0.3–10 µM) to the longitudinal and circular muscle strips of the rumen did not induce any change in tension or electric field stimulation-induced phasic contractions of the muscle strips. These results demonstrated that circulating xenin-25 stimulates rumen contractions by acting on sites except the intramural intrinsic nerve plexus or smooth muscles of the rumen, implying that xenin-25 acts on the gastric center and/or cholinergic efferent nerve innervated to the ovine rumen.

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最終責任者 Takenori Onaga (First Author and Corresponding Author)



Contents lists available at

General and Comparative Endocrinology





Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep

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ARTICLEINFO

Reywords:
Pancreas
Ensyme
Bicarbonste
Cholinergic nerve
Neurotensin receptor
Antagonist

ABSTRACT

The present study aimed to clarify the effects of neurotensin and xenin on pancreatic exocrine securiton in conscious sheep and their mechanism of actions. The animals were equipped with two silastic cannulse in the common bile duct to separately collect pancreatic fluid and bile, and a silastic cannula in the proximal duodenum to continuously return the mixed fluids. NT and xenin were intravenously injected at range of 0.01-3.0 nmol/kg during the phase I of disodenal migrating motor complex. A single intravenous NT injection significantly and dose-dependently increased pancreatic fluid, protein, and bicarbonate outputs. The effect of NT at 1 nmol/kg was completely inhibited by a background intravenous infusion of atropine methyl nitrate at a dose of 10 nmel/kg/ min, however, the effect was not altered by a prior injection of the neurotensin receptor subtype (NTR)-1 antagonist SR 48692 at 60 nmol/kg. Moreover, a single intravenous xenin-25 injection significantly and dosedependently increased pancreatic fluid and protein output, whereas the effect of xenin-25 did not clearly show dose-dependence. The prior SR 48692 injection at 30 nmol/kg did not significantly alter the effects of xenin-25 at 0.3 nmol/kg, while the atropine infusion significantly inhibited the increase in fluid secretion. Under the acropine infusion, xenin-25 at 0.3 nmol/kg did not increase protein and bicarbonate outputs, whereas the inhibitory effect of the atropine was not significant compared to that of the single injection of xenin-25. A single intraveasous injection of NTR-2 agonist levocabastine at 0.1-3 nmol/kg did not alter pancreatic exocrine secretion. These results suggest that both NT and xenin-25 effectively stimulates pancreatic exocrine secretion through the peripheral cholinergic system in sheep and that NTR-2 is not involved in the regulation of pancreatic exocrine secretion, however, we did not precisely determine the role of NTR-1 in the actions of both the peptides on pancreatic execrine secretion.

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Assessment of hypoxia-targeting therapy for gastrointestinal lymphoma in dogs: Preclinical test using murine models.

Yamazaki H, Tanaka T, Nishida H, Hatoya S, Akiyoshi H.

Res Vet Sci. 154:22-28. 2022. doi: 10.1016/j.rvsc.2022.11.003

2) Hypoxia-targeting therapy for intestinal T-cell lymphoma in dogs: Preclinical study using 3D in vitro models.

Yamazaki H, Tanaka T, Nishida H, Hatoya S, Akiyoshi H.

Vet Comp Oncol. In press. 2022. doi: 10.1111/vco.12855.

3) Single-modality palliative radiotherapy versus palliative radiotherapy after chemotherapy failure for cats with nasal lymphoma.

Yamazaki H, Wada Y, Tanaka T, Noguchi S.

Vet Radiol Ultrasound. 63:498-505. 2022. doi: 10.1111/vru.13075.

II. その他<Others>

- 1) Comparing the CT and MRI findings for canine primary hepatocellular lesions. Kurokawa S, Tanaka T, **Yamazaki H**, Noguchi S, Wada Y, Nishida H, Akiyoshi H. *Vet Rec.*;190:e1083. 2022. doi: 10.1002/vetr.1083.
- 2) Computed tomography and magnetic resonance imaging findings in dogs with vaginal leiomyoma and leiomyosarcoma.

Tanaka T, Noguchi S, Wada Y, <u>Yamazaki H</u>, Nishida H, Akiyoshi H.

Vet Med Sci. 8:2337-2344. 2022. doi: 10.1002/vms3.930.



Research in Veterinary Science Volume 154, January 2023, Pages 22-28



Assessment of hypoxia-targeting therapy for gastrointestinal lymphoma in dogs: Preclinical test using murine models

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Abstract

The transcription factor hypoxia-inducible factor 10 (HIF-10) is expressed in several camoers under intratamoral hypoxic stress that arises during pathogenic processes, resulting in malignant progression. We previously reported that hypoxic stimulation enhances the growth potential of canine lymphoma cells by activating the HIF-1a signaling pathway. In contrast, evofosfamide (Evo) releases a DNAalkylating molety within hypoxic tumor regions, suggesting that Evo could serve as a hypoxia-targeting drug in canine lymphoma. This study aimed to use Evo to evaluate hypoxia-targeted therapy in dogs with gastrointestinal lymphoma (GIL) and investigate how Evo affects antibumor efficacy and adverse events in three type of marine senograft models using T-cell GIL cells. In vitro tests, the sensitivity to Evo of three T-cell GIL cell lines under hypoxic culture was significantly higher than that under normoxic culture. Our metabolic analysis suggested that the three murine models might have high reproducibility as clinical cases in canine GIL. Our data showed that Evo showed significantly higher tumor growth potential and fewer adverse events in three type of murine models compared to lomustine; CeeNu (CCNU). Additionally, Evo suppressed the expression of HIF-1a protein in tumor tissues, suggesting that it may preferentially target and inhibit tumor cells in a hypoxic region. The evidence presented here supports the favorable preclinical evaluation that Evo may be effective for GB, in dogs.

出典 doi: 10.1016/j.rvsc.2022.11.003.

https://www.sciencedirect.com/science/article/abs/pii/S0034528822003605?via%3Dihub 最終責任者 Hiroki Yamazaki (First Author and Corresponding Author)

Veterinary and Comparative Oncology

ORIGINAL ARTICLE

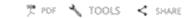
Hypoxia-targeting therapy for intestinal T-cell lymphoma in dogs: Preclinical study using 3D in vitro models

Hiroki Yamazaki 🐹 Toshiyuki Tanaka, Hidetaka Nishida, Shingo Hatoya, Hideo Akiyoshi

First published: 11 August 2022 | https://doi.org/10.1111/vco.12855

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Abstract

The transcription factor hypoxia-inducible factor 1a (HIF-1a) is activated in response to oxygen deficiency, and is expressed in several cancers under intratumoral hypoxic stress that arises during pathogenic processes. Hypoxic stimulation enhanced the growth potential of canine lymphoma cells by activating the HIF-1a signalling pathway in a previously reported study. The aim of this study was to establish a molecular design strategy for a novel hypoxia-targeting therapy for intestinal T-cell lymphoma (ITL) in dogs. We assessed the relationship between immunohistochemistry-based HIF-1a expression and clinical information, including signalment, tumour area, clinical signs, systemic diseases, treatment protocol, follow-up information, chemotherapy response and overall survivals (OS), using 48 tissue samples from dogs with ITL. We investigated the effects of hypoxic stimulation on the biological behaviour of cell lines from three different types of canine ITL. We assessed the effects of evofosfamide (Evo; hypoxia-activated prodrug) on cell lines cultured under hypoxic conditions. Our data showed that treatment response and overall survival might be significantly decreased in dogs with higher HIF-1a expression than in those with lower HIF-1a expression. Hypoxic culture (1% O₂, 72 h) enhanced the invasiveness of cell lines and decreased their sensitivity to CCNU, resulting in hypoxia-dependent aggressive behaviour. Sensitivity to Evo significantly increased in cell lines cultured under hypoxia compared with those cultured under normoxia, which exhibited hypoxia-dependent apoptosis. Additionally, Evo downregulated HIF-1a expression in cell lines cultured under hypoxia, suggesting that Evo might inhibit cell growth by inactivating HIF-1a-dependent cell signalling. Our results revealed the preclinical antitumor activity of Evo and provide a rationale for treatment strategies for dogs with ITL.

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最終責任者 Hiroki Yamazaki (First Author and Corresponding Author)



Veterinary Radiology & Ultrasound



ORIGINAL INVESTIGATION

Single-modality palliative radiotherapy versus palliative radiotherapy after chemotherapy failure for cats with nasal lymphoma

Hiroki Yamazaki, Yusuke Wada, Toshiyuki Tanaka, Shunsuke Noguchi 🖾

First published: 21 February 2022 | https://doi.org/10.1111/vru.13075

Previous presentation/publication disclosure: : Preliminary results of this study were presented and published at the Veterinary Cancer Society Virtual Annual Conference in October 17th, 2020. Reporting guideline checklist disclosure: : The VRU "Technical Information for Radiation Therapy" reporting guidelines were followed.

Read the full text >







Abstract

Published studies describing outcomes for cats with nasal lymphoma (NLSA) receiving first-line palliative radiation (PRT) versus PRT after chemotherapy failure are currently lacking. The aims of this retrospective observational study were to compare outcomes for cats with NLSA that were treated with these two methods. A total of 48 cats were included in analyses; 32 receiving PRT alone and 16 receiving PRT after chemotherapy failure. The treatment response, progression-free survival (PFS), disease-specific survival (DSS), overall survival (OS), and incidence rate of systemic disease were compared between the two groups. The overall response rate (ORR) was calculated from the same target lesions between pre-RT (within a week before starting PRT) and post-RT (on date of PRT completion) by computed tomography (CT) imaging. The ORR was 94% in cats that received PRT alone, 13 had a complete response (CR) and 17 had a partial response (PR). The ORR was 88% in cats that received PRT after chemotherapy failure, with five having CR and nine with PR. There were no significant differences in the ORR between the two groups. The PFS, DSS, and OS significantly increased in the cats that received PRT alone compared to the cats that received PRT after chemotherapy failure (median PFS: 336 vs 228 days, P = 0.0012, median DSS: 360 vs 242 days, P = 0.0025, median OS: 346 vs 242 days, P = 0.0036, respectively). The incidence rate of systemic disease significantly increased in 75% (12/16) of cats receiving PRT after chemotherapy failure compared to 41% (13/32) of cats receiving PRT alone. The results suggested that clinical outcomes may improve in cats with NLSA with first-line PRT compared to PRT after chemotherapy failure.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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最終責任者 Shunsuke Noguchi (Corresponding Author)

VetRecord

Original research

Comparing the CT and MRI findings for canine primary hepatocellular lesions

Shohei Kurokawa, Toshiyuki Tanaka, Hiroki Yamazaki, Shunsuke Noguchi, Yusuke Wada, Hidetaka Nishida, Hideo Akiyoshi 😭

First published: 08 November 2021 | https://doi.org/10.1002/vetr.1083

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Abstract

Background

Triple-phase CT and gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) MRI have been used to differentiate hepatocellular carcinomas (HCCs) in dogs.

Methods

This retrospective case series aimed to compare the CT findings with MRI findings of 20 canine hepatocellular lesions, including eight poorly/moderately-differentiated HCCs, eight well-differentiated HCCs and four hyperplasias. CT data were analysed, and the following parameters were noted: vessel enhancement, enhancement pattern in the equilibrium phase, maximal transverse diameter, the lowest enhancement, and the attenuation values of each hepatocellular lesion in the precontrast and triple-phase series, including the arterial phase, portal phase and equilibrium phase. MRI data were analysed, and the following parameters were noted: signal intensities of each hepatocellular lesion on T2-weighted images and T1-weighted images, and signal intensity ratio of the hepatocellular lesions in the hepatobiliary phase.

Results

In 62.5% of poorly/moderately-differentiated HCC and 75% of well-differentiated HCC, presumptive necrosis was detected on CT and MRI. In the hepatobiliary phase on MRI, the median signal intensity ratio of poorly/moderately-differentiated HCC (0.54 [range: 0.3–0.71]) was significantly lower than that of well-differentiated HCC (0.75 [range: 0.6–0.96]) and hyperplasia (0.79 [range: 071–0.98]; $p \approx 0.02$ and $p \approx 0.02$, respectively).

Conclusion

Gd-EOB-DTPA-enhanced MRI may be a superior modality for differentiating hepatocellular origin lesions.

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最終責任者 Hideo Akiyoshi (Corresponding Author)

Veterinary Medicine and Science

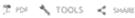
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Computed tomography and magnetic resonance imaging findings in dogs with vaginal leiomyoma and leiomyosarcoma

Toshiyuki Tanaka, Shunsuke Noguchi, Yusuke Wada, Hiroki Yamazaki, Hidetaka Nishida, Hideo Akiyoshi 🐯

First published: QS September 2022 | https://doi.org/10.1002/vms3.930





Abstract

Background

in humans, magnetic resonance imaging (MRI) is preferred over computed tomography (CT) for the assessment of pelvic lesions, Although CT findings of several pelvic tumours have been reported in veterinary medicine, MRI findings are limited.

Objectives

The purpose of this study was to retrospectively compare the CT and MRI findings in dogs with vaginal leiomyoma and leiomyosarcoma.

Methods

This retrospective study of five dogs compared the CT and MRI findings of intrapelvic lesions, including vaginal leiomyoma (n = 4) and leiomyosarcoma (n = 1). No invasion of the surrounding tissue was detected on histopathological examination. In this retrospective study, the following parameters of CT and MRI were recorded for each dog: the border between the lesion and the adjacent pelvic organs, including the prostate, rectum or urethra; signal intensity (SI) of the lesion; enhancement pattern; presence of haemorrhage; necrosis or cystic areas and lymphadenopathy. Because SI on MRI is affected by cell density, tumour cell density was analysed using a microscope säde.

Results

In vaginal leiomyoma, the border between the lesion and the surrounding pelvic organ tends to be clearer on MRI than on CT, in vaginal leiomyosarcoma, the border was comparable between MRI and CT. Each lesion showed heterogeneous enhancement on CT and MRI scans. In each lesion, the assessment of haemorrhage, necrosis, cystic areas and lymphadenopathy was comparable between MRI and CT. The SI of the lesion on T2WI of the vaginal leiomyoma and leiomyosarcoma were hyperintense in four cases (4/4; 100%) and mixed intense in one case (1/1; 100%), respectively. The cell density of lelomyosarcoma is higher than that of lelomyomas.

Conclusions

The SI on T2WI may be useful for differentiating leiomyoma from leiomyosarcoma. MRI may be useful to differentiate vaginal leiomyomas from leiomyosarcomas and evaluate margins.

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獣医解剖学 (Veterinary Anatomy)

Takafumi Watanabe

Associate Professor

准教授 渡邉 敬文

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Morphological analysis of cell distribution and network structure via gap junctions in swine corneal stroma.

Hoshino N, Takehana K, Hosotani M, Kametani K, Iwasaki T, Hasegawa Y, Ueda H, **Watanabe T**.

J. Vet. Med. Sci. 84(12):1621-1632. 2022. doi: 10.1292/jvms.22-0329.

2) Three-dimensional structural analysis of mitochondria composing each subtype of fasttwitch muscle fibers in chicken.

Makida S, Kametani K, Hosotani M, Takahashi N, Iwasaki T, Hasegawa Y, Takaya T, Ueda H, **Watanabe T.**

J. Vet. Med. Sci. 84(6):809-816. 2022. doi: 10.1292/jvms.22-0080.

II. その他<Others>

1) The histopathological features of the surgical endometriosis model using systemic autoimmune disease-prone mice.

Hosotani M, Akita M, Ueda H, Watanabe T.

J. Vet. Med. Sci. Nov 28. 2022. doi: 10.1292/jvms.22-0442.

2) Mitochondrial characteristics of chicken breast muscle affected by wooden breast. Hasegawa Y, Hosotani M, Saito M, Nagasawa T, Mori Y, Kawasaki T, Yamada M, Maeda N, Watanabe T, Iwasaki T.

Comp Biochem Physiol A Mol Integr Physiol. 273: 111296-111296. 2022 doi: 10.1016/j.cbpa.2022.111296.

3) The location of protein oxidation in dystrophic skeletal muscle from the mdx mouse model of Duchenne muscular dystrophy.

Iwasaki T, Terrill R J, Kawarai K, Miyata Y, Tagami T, Maeda N, Hasegawa Y, **Watanabe T**, Grounds D M, Arthur G P.

Acta. histochemical. 124(8): 151959-151959 2022. doi: 10.1016/j.acthis.2022.

4) Clinical and pathophysiological delineation of musculocontractural Ehlers-Danlos syndrome caused by dermatan sulfate epimerase deficiency (mcEDS-DSE): a detailed and comprehensive glycobiological and pathological investigation in a novel patient.

Minatogawa M, Hirose T, Mizumoto S, Yamaguchi T, Nagae C, Taki M, Yamada S,

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Hum. Mutat. 43(12):1829-1836. 2022. doi: 10.1002/humu.24437.

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Kawasaki T, Iwasaki T, <u>Watanabe T</u>, Hasegawa Y, Hosotani M, Yamada M.

J. Poult. Sci. 59(4):378-383. 2022. doi: 10.2141/jpsa.0220029.



FULL PAPER

Anatomy

Morphological analysis of cell distribution and network structure via gap junctions in swine corneal stroma

Nobutaka HOSHINO¹⁾, Kazushige TAKEHANA¹⁾, Marina HOSOTANI¹⁾, Kiyokazu KAMETANI¹⁾, Tomohito IWASAKI²⁾, Yasuhiro HASEGAWA²⁾, Hiromi UEDA¹⁾, Takafumi WATANABE¹⁾*

ABSTRACT. Because of corneal transplantation limitations, there is a need for cornea-specific regenerative medicine. The development of such regenerative medicine has been delayed because of the complex and unique structure of the corneal stroma. Few studies have explored the corneal stroma cell distribution and cell types in vivo. This study investigated regional differences in morphological characteristics and distributions of corneal keratocytes and immunocompetent cells in the corneal stroma to clarify their functions and structural characteristics. The porcine eyeballs were subjected to light microscopy, transmission electron microscopy, scanning electron microscopy, and immunofluorescence staining analyses. Corneal cells were primarily located in the limbus, rather than the center of the cornea; the long keratocyte diameter was largest on the epithelial side of the corneal limbus, while the short diameter was largest on the endothelial side of the central cornea, Moreover, there were significantly more corneal cells on the epithelial side than on the endothelial side in both the central and limbus areas. Gap junctions between cells in the corneal stroma were present on the surfaces of cytoplasmic processes. Many cytoplasmic processes were scattered throughout the corneal stroma; they were connected both vertically and horizontally, forming an intercellular network. Additionally, immunocompetent cells on the epithelial side suggested to participate in this network via gap junctions. The morphology of keratocytes and immunocompetent cells on the epithelial side suggests that they play important roles in corneal homeostasis.

KEYWORDS: corneal keratocytes, corneal stroma, electron microscopy, gap junction, swine

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FULL PAPER

Anatomy

Three-dimensional structural analysis of mitochondria composing each subtype of fast-twitch muscle fibers in chicken

Sachi MAKIDA¹⁾, Kiyokazu KAMETANI¹⁾, Marina HOSOTANI¹⁾, Naoki TAKAHASHI²⁾, Tomohito IWASAKI³⁾, Yasuhiro HASEGAWA³⁾, Tomohide TAKAYA⁴⁾. Hiromi UEDA¹⁾ and Takafumi WATANABE^{1)*}

ARSTRACT. In a previous study, the three-dimensional structures of mitochondria in type I and type IIb muscle fibers of chicken were analyzed. The study reported differences in the shape of the mitochondria and the distribution of lipid droplets. In this study, we three-dimensionally analyzed mitochondria and lipid droplets of type II muscle fiber subtypes IIa, IIb, and IIc of chicken lateral iliotibial muscle in the same field of view using correlative light electron microscopy (CLEM) and array tomography methods. The reconstructed images showed that the mitochondria of type IIa muscle fiber were thick and aligned along the myofibrils, and many lipid droplets were embedded in the mitochondria. The mitochondria of type IIb muscle fibers were intermittent, aligned along the myofibrils, and showed contact between adjacent horizontal mitochondria. No lipid droplets were observed in type IIb muscle fiber. In type IIc muscle fiber, we observed irregularly shaped mitochondria with small diameters aligned along the myofibrils. Lipid droplets not only were embedded in the mitochondria but also existed independently in some cases. The combination of array tomography and CLEM methods enabled three-dimensional electron microscopic observation of mitochondria in different subtypes of type II muscle fibers. The subtypes of type II muscle fibers differed in mitochondrial occupancy and morphology and in lipid droplet distribution, and characteristics that had been demonstrated blochemically were also demonstrated ultrastructurally.

KEYWORDS: array tomography, correlative light electron microscopy, electron microscopy, fast skeletal muscle, mitochondria

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The histopathological features of the surgical endometriosis model using systemic autoimmune disease-prone mice

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Author information

Keywords: autoimmune disease, endometriosis, immune cell, surgical model, uterus

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T Details

Article overview

- Abstract
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Abstract

Endometriosis is a common gynecological disease that affects women of reproductive age in which the uterine endometrium grows outside the uterus. Origin of the ectopic endometrium is thought to be the retrograde endometrium through the oviducts. However, factors that determine the adherence and proliferation of the ectopic endometrium have not been revealed. Importantly, systemic autoimmune diseases are considered a key factor in the endometriosis onset. Herein, we established a surgical endometriosis rodent model using autoimmune disease-prone MRL/MpJ-Fasion/lpr (MRL/lpr) and MRL/+ mice to provide basic evidence of the relationship between autoimmune disease and endometriosis. Endometriosis lesions were successfully induced in two regions after transplanting uterine tissues from donor mice into the peritoneal cavity of recipient mice: the peritoneum or adipose tissue around the transplantation point (proximal lesions) and the gastrosplenic ligament or intestinal mesentery far from the transplantation site (distal lesions). Distal lesions were observed only in MRL/lpr mice, whereas endometriosis lesions showed no genotype- or regionrelated differences in the histology and distribution of sex hormone receptors and Ticells. In contrast, transplanted uterine tissues in donor MRL/lpr mice exhibited a large infiltration of Ticells in the lamina propria. Splenomegaly was more common in recipient than that in donor MRL/lpr mice. These results suggest that the infiltration of endogenous T cells in the endometrium alters the growth features of ectopic endometrium, possibly affecting the severity of endometriosis in patients with systemic autoimmune diseases.

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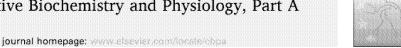
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最終責任者 Marina Hosotani (Corresponding Author)



Contents lists available at accessor linear

Comparative Biochemistry and Physiology, Part A







Mitochondrial characteristics of chicken breast muscle affected by wooden breast

Yasuhiro Hasegawa a, Marina Hosotani b, Miyu Saito a, Tatsuki Nagasawa a, Yusuke Mori a, Takeshi Kawasaki , Michi Yamada , Naoyuki Maeda , Takafumi Watanabe Tomohito Iwasaki a,

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ARTICLE INFO

Edited by Michael Hedrick

Keywords: Antioxidant enzyme Reactive oxygen species SOD1 and SOD2

ABSTRACT

The growth rate of broiler chickens has increased by 400% over the past 50 years, and breast yields continue to increase. This has led to an increase in thoracic muscle abnormalities in broilers, with wooden breast becoming a major issue worldwide. The etiology and the mechanism underlying the etiology of wooden breasts have not yet been elucidated; however, it occurs due to oxidative stress. Reactive oxygen species, which cause oxidative stress, are mainly produced in mitochondria. Thus, in this study, we investigated the relationship between the severity of wooden breast in broilers and the characteristics of mitochondria as the source of reactive oxygen species. Sampling of the pectoralis major muscle at the ventral cranial position was conducted in 50-day-old broilers. The severity of wooden breast was classified into three groups based on the muscle fiber roundness and wing-wing contact test, with highest severity in severe wooden breast and lowest severity in normal breast. Nicotinamide adenine dinucleotide tetrazolium reductase staining revealed an increase in darkly stained muscle fibers, indicating high severity of wooden breast. The mitochondria were swollen in severe wooden breast cases, with highest swelling in severe wooden breast and lowest swelling in normal breast. The expression levels of the mitochondrial antioxidant enzyme genes superoxide dismutase 1 and superoxide dismutase 2 were significantly lower in wooden breast-severe tissue than in normal tissue. These results suggest that when the levels of reactive oxygen species in muscle fibers, which should be constant, are increased, mitochondrial homeostasis is not maintained and the damage levels increase in various membranes of the cell, leading to the disruption of normal physiological functions.

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https://www.sciencedirect.com/science/article/pii/S1095643322001544?via%3Dihub

最終責任者 Tomohito Iwasaki (Corresponding Author)



Contents lists available at ScienceDirect

Acta Histochemica







The location of protein oxidation in dystrophic skeletal muscle from the *mdx* mouse model of Duchenne muscular dystrophy

Tomohito Iwasaki ^a, Jessica R. Terrill ^b, ^{*}, Kei Kawarai ^a, Yusei Miyata ^a, Takayoshi Tagami ^c, Naoyuki Maeda ^a, Yasuhiro Hasegawa ^a, Takafumi Watanabe ^d, Miranda D. Grounds ^c, Peter G. Arthur ^b

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ARTICLEINFO

Represents: max mice Myonecrosis Dystrophic muscle Oxidised proteins RONS Dityrosines DMD

ABSTRACT

Duchenne muscular dystrophy (DMD) is a severe childhood disease characterised by progressive muscle wasting caused by widespread myofibre necrosis. Implicated in the pathology of DMD is oxidative stress, caused by excessive generation of reactive oxygen and nitrogen species (RONS). One consequence of RONS exposure is post-translational oxidative modifications to proteins, which can cause loss of protein function. This study used the dystrophic mdx mouse model for DMD to visualise the precise location of different oxidative modifications to proteins in dystrophic muscles, including both reversible (protein thiol oxidation and s-nitrosylation) and irreversible (carbonylation and dityrosine formation) oxidation at various stages of dystrophic muscle necrosis and regeneration. High levels of protein oxidation were observed in mdx myofibres undergoing degeneration and immune cell infiltration (myonecrosis). Since irreversible protein oxidation, especially dityrosine formation, was only colocalised to areas of myonecrosis, we suggest that this specific measurement could be a useful biomarker of myonecrosis. To test this we quantified dityrosines in muscle homogenates; this analysis showed significantly higher levels of dityrosines in max (compared with control normal) mice aged 23 days, an age when acute onset of extensive myonecrosis occurs in mdx muscles. These results indicate a major localised role of immune cells in RONS generation in dystrophic muscle, and strongly support a role for protein oxidation in myonecrosis and associated dystropathology. Consequently, the measurement of protein oxidation (specifically dityrosines) in dystrophic muscles may be a useful biomarker for indirectly quantifying myonecrosis in research studies using mdx mice and other animal models for DMD.

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最終責任者 Terrill R. Jessica (Corresponding Author)



BRIEF REPORT

Clinical and pathophysiological delineation of musculocontractural Ehlers-Danlos syndrome caused by dermatan sulfate epimerase deficiency (mcEDS-DSE): A detailed and comprehensive glycobiological and pathological investigation in a novel patient

Mari Minatogawa, Takuya Hirose, Shuji Mizumoto, Tomomi Yamaguchi, Chiai Nagae, Masashi Taki, Shuhei Yamada, Takafumi Watanabe, Tomoki Kosho 🔀

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Mari Minatogawa, Takuya Hirose, and Shuji Mizumoto contributed equally to this study.

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Abstract

Musculocontractural Ehlers–Danlos syndrome caused by dermatan sulfate epimerase deficiency (mcEDS-DSE) is a rare connective tissue disorder. This is the first report describing the detailed and comprehensive clinical and pathophysiological features of mcEDS-DSE. The patient, with a novel homozygous nonsense variant (NM_013352.4:c.2601C>A:p.(Tyr867*)), exhibited mild skin hyperextensibility without fragility and small joint hypermobility, but developed recurrent large subcutaneous hematomas. Dermatan sulfate (DS) moieties on chondroitin sulfate/DS proteoglycans were significantly decreased, but remained present, in skin fibroblasts. Electron microscopy examination of skin specimens, including cupromeronic blue-staining to visualize glycosaminoglycan (GAG) chains, revealed coexistence of normally assembled collagen fibrils with attached curved GAG chains and dispersed collagen fibrils with linear GAG chains from attached collagen fibrils across interfibrillar spaces to adjacent fibrils. Residual activity of DS-epi1, encoded by DSE, and/or compensation by DS-epi2, a minor homolog of DS-epi1, may contribute to the mild skin involvement through this "mosaic" pattern of collagen fibril assembly.

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≪Research Note≫

Immune Response in Chickens Vaccinated with Freeze-Thawed or Warmed Water-in-Oil Vaccine

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This study investigated whether freezing or warming water-in-oil (W/O) vaccines affected the immune responses of chickens. One of the conditions affecting the efficacy of commercially available animal vaccines is the storage temperature range. Previous studies have shown that the properties of some inactivated vaccines change owing to freezing, leading to reduced immune responsiveness after inoculation. In this study, we first determined the freezing temperatures of a commercial W/O vaccine using freezers maintained at -10, -13, -15, and -20° C. The results showed that the W/O vaccine froze from -10 to -12° C. Next, we evaluated the effect on antibody level transitions (sample-to-positive ratio) in 46-day-old broiler chickens vaccinated with the W/O vaccine that was maintained at -20° C, 5° C, and -10° C, in that order. In addition, the effect on antibody value transitions was evaluated in 45-day-old broiler chickens vaccinated with the W/O vaccines that were frozen and thawed between -20° C and 5° C repeatedly or warmed to 42° C. In these experiments, no remarkable effect of the freeze-thawing or warming treatments on antibody value transitions was observed. These results suggested that the efficacy of the W/O vaccine was not significantly affected when placed in a frozen environment or left in a room temperature environment of 42° C or lower for approximately 5 d. These data indicate the possibility of expanding the temperature range for handling W/O vaccines.

Key words: adjuvant, cold chain, freeze-thaw, handling temperature, storage temperature, water-in-oil vaccine
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GENOME SEQUENCES
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Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

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ABSTRACT Bovine pneumonia is a disease that causes significant economic losses in livestock industries and is vital for animal welfare. The whole-genome sequence of *Pasteurella multocida* strain Pm1, isolated from a calf suffering from pneumonia in Japan, is reported here.

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最終責任者 Hidetoshi Higuchi (Corresponding Author)



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Research paper

Effects of intra-articular inoculation with Mycoplasma bovis on immunological responses in calf joints



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Keywords Inflammatory cytokines Invasion Matrix metalloproteinases Mycoplasma bovis

ABSTRACT

Mycoplasma arthritis that caused by Mycoplasma bovis exhibit severe lameness. This disease is difficult to cure with antibiotics, but the detailed pathological mechanisms have not been fully clarified. In this study, we examined the effects of intra-articular inoculation with M. bovis on immunological responses in calf joints. We inoculated three calves each with M. bovis or phosphate buffer saline (control) into the right stifle joint and dissected them at 15 days postinoculation. Mycoplasma bovis-inoculated calves exhibited swelling of the stifle joint, increases in synovial fluid, fibrin deposition, and cartilage thinning. Intracellular M. bovis was detected in synovial tissues analyzed by immunohistochemistry and transmission electron microscopy. Messenger RNA expressions of interleukin (IL)-1β, IL-6, IL-8, IL-12p40, and IL-17A in synovial fluid cells and synovial tissues from M. bovis-inoculated calves were significantly higher than those from control calves. Protein levels of these cytokines in synovial fluid from M. bovis-inoculated calves were markedly higher than those from control calves. Our study clarified that inoculation with M. bovis into the stifle joint induced the production of inflammatory cytokines by synovial fluid cells and synovial tissues, causing a severe inflammatory response in joints. Additionally, M. bovis could invade cells in synovial tissues, which may have aided it in evading antibiotics and host immune surveillance.

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RESEARCH ARTICLE



Evaluation of the health status of mammary glands and compositional changes in udder-half milk obtained from dairy goats for milk quality management

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Abstract

This study evaluated the health status of the mammary glands and milk composition of dairy goats. The California mastitis test (CMT) score, somatic cell counts (SCCs), somatic cell type, electrical conductivity (EC), N-acetyl-p-o-glucosaminidase (NAGase) activity, mastitis-causing pathogens, and milk composition in 121 udderhalf milk samples from 62 crossbreed goats (1-3 years old) at 23-45 days postpartum were compared in four categories with SCCs of <200 × 103, $<300 \times 10^{3}$, $301-1000 \times 10^{3}$, and $>1010 \times 10^{3}$ cells/ml. The SCC, CMT score, EC. and NAGase activity were significantly lower (p < 0.05) in udder-half milk with SCCs of $<200 \times 10^3$ and $<300 \times 10^3$ cells/ml than those in milk with SCCs of 301- 1000×10^3 and $>1010 \times 10^3$ cells/ml. The protein, lactose/ash, and solids-not-fat (SNF) in milk with an SCC of $<300 \times 10^3$ cells/ml were similar to the previously reported values. The proportion of polymorphonuclear neutrophils was significantly higher (p < 0.05) in milk with SCCs of 301–1000 and >1010 \times 10³ cells/ml than in milk with an SCC of $<300 \times 10^3$ cells/ml. Assessing mammary gland health and milk composition based on categorization of udder-half milk by SCC may be useful for milk quality control on goat farms.

KEYWORDS

dairy goat, mammary health parameters, milk composition, quality control

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scientific reports



OPEN Biological properties of *Staphylococcus* virus ΦSA012 for phage therapy

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Staphylococcus virus ФSA012 has a wide host range and efficient lytic activity. Here, we assessed the biological stability of ФSA012 against temperature, freeze-thawing, and pH to clinically apply the phage. In addition, inoculation of ФSA012 through i.p. and i.v. injections into mice revealed that phages were reached the limit of detection in serum and accumulated notably spleens without inflammation at 48 h post-inoculation. Furthermore, inoculation of ФSA012 through s.c. injections in mice significantly induced IgG, which possesses neutralizing activity against ФSA012 and other Staphylococcus viruses, ФSA039 and ФMR003, but not Pseudomonas viruses ФS12-3 and ФR18 or Escherichia virusesT1, T4, and T7 in vitro. Immunoelectron microscopic analysis showed that purified anti-phage IgG recognizes the long-tail fiber of staphylococcus viruses. Although 5. aureus inoculation resulted in a 25% survival rate in a mouse i.p. model, ФSA012 inoculation (i.p.) improved the survival rate to 75%; however, the survival rate of ФSA012-immunized mice decreased to less than non-immunized mice with phage i.v. injection at a MOI of 100. These results indicated that ФSA012 possesses promise for use against staphylococcal infections but we should carefully address the appropriate dose and periods of phage administration. Our findings facilitate understandings of staphylococcus viruses for phage therapy.

Staphylococcus aureus, which is a gram-positive bacterium that inhabits animals and humans, has high pathogenicity and causes severe infectious diseases. Mortality rates in humans are higher than 30% in cases of severe systemic infections. Healthcare-associated S. aureus causes a variety of infections such as respiratory, urinary tract, surgical-associated, and blood stream infections through long-term hospital stays, whereas community-associated S. aureus causes skin and soft tissue infections in healthy people who have no association with hospital care. In addition, livestock-associated S. aureus is one of the most frequent pathogens involved in subclinical and clinical bovine mastitis, leading to economic losses of \$100 million every year due to decreased milk production in the United States and Japan. Therefore, successful prevention and treatment of S. aureus infections would have great impacts not only on human health, but also industry. 5.

Infectious diseases caused by antimicrobial-resistant bacteria have considerable negative impacts on public health. O'Neill et al. estimated that 10 million people will die annually due to antimicrobial-resistant bacterial infections by 2050 without a global program against antimicrobial resistance (AMR)⁶. Notably, S. aureus is classified as an ESKAPE pathogen (other examples of which include Enterococcus faecium, S. aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, and Enterobacter spp.) that are frequently isolated

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ORIGINAL PAPER



A novel polymerase chain reaction assay for the detection of seven *Mycoplasma* species of cattle origin

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Abstract

The study aimed to develop a pair of polymerase chain reaction primers for detecting ruminant mycoplasma pathogens. We designed a set of primers based on the most similar sequences within 16 S rRNA regions of seven Mycoplasma spp. These primers have high sensitivity for detecting Mycoplasma dispar, M. arginine, M. canadense, M. bovis, M. alkalescens, M. californicum, and M. bovigenitalium within the annealing temperature range of 46 to 48 °C. The minimum amount of DNA that can be detected using the protocol is 250 ng, which is equivalent to 2,000 colony-forming units per mL. The primers can detect mycoplasma from DNA extracted directly from milk samples. The common bovine mastitis pathogens of Staphylococcus aureus coagulase-negative staphylococci, Escherichia coli, Streptococcus uberis, Klebsiella pneumonia, and Kocuria rosea were not detected by the primers. We believe the high sensitivity and specificity of these primers make them useful for detecting infection with seven Mycoplasma species in ruminants, allowing the primers to be used in clinical settings.

Keywords Mycoplasma · Polymerase chain reaction · Bovine

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最終責任者 Jyhmirn Lai (First Author and Corresponding Author)



SHORT COMMUNICATION

Experimental Research

Comparing chemiluminescent response and intracellular bactericidal activity of bovine blood neutrophils and monocytes against Salmonella Dublin and Escherichia coli

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Abstract

Chemiluminescent (CL) response and the intracellular killing activity of polymorphonuclear neutrophils (PMNs) and monocytes (MOs) from healthy calves were evaluated to clarify the responsiveness of phagocytes to Salmonella Dublin (S. Dublin) and Escherichia coli (E. coli). CL responses of PMNs and MOs against S. Dublin and E. coli were significantly lower (P < 0.05) than that with opsonized zymosan. The intracellular bactericidal activity of PMNs and MOs was found to be effective against E. coli but not against S. Dublin. These findings indicated that the bactericidal activity of bovine PMNs and MOs against S. Dublin was impaired in innate immune response and that a decreased killing activity against S. Dublin could be a contributing factor for chronic salmonellosis in cattle.

Key Words: bovine monocytes, intracellular bactericidal activity, Salmonella Dublin

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RESEARCH ARTICLE



Sodium butyrate administration modulates the ruminal villus height, inflammation-related gene expression, and plasma hormones concentration in dry cows fed a high-fiber diet

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Abstract

The objectives of this study were to evaluate the effects of sodium butyrate on the ruminal villus morphology, mRNA expression associated with nutrient metabolism and inflammation in the ruminal epithelium, and plasma concentrations of metabolites and hormones in non-lactating cows fed a high-fiber diet. Four Holstein cows with a rumen cannula were assigned to two treatments in a crossover design. The treatments were ruminal administration of sodium butyrate premix or control premix before feeding to cows fed the same total mixed ration mainly composed of glass silage once a day. Sodium butyrate was provided at a butyrate dose of 0,04% per kg body weight. The control premix was made by replacing sodium-butyrate with wheat bran. The plasma β-hydroxybutyrate concentration increased 3 to 6 h after the butyrate premix administration but returned to a concentration similar to that of the control before feeding. After continuous administration, increases in the ruminal villus height and plasma concentration of glucagon-like peptide-2, and lower gene expression of TNF- α , IL-1 β , and TLR-2 in the rumen epithelium were observed in cows supplied with the butyrate premix. These results showed that sodium butyrate affects rumen epithelial morphology and plasma concentrations of hormones even under a low fermentable diet.

KEYWORDS

butyrate, dairy cow, GLP-2, inflammation-related gene, rumen papillae

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- Case Report: Usefulness of Drip Infusion Cholangiography With Computed Tomography for the Diagnosis of Biloma in a Dog

Tamura M, Ohta H, Hasegawa N, Hosoya K, Takiguchi M.

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2) Visualising the hepatic vascular architecture using superb microvascular imaging in a dog with severe hepatic fibrosis

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Case Report: Usefulness of Drip Infusion Cholangiography With Computed Tomography for the Diagnosis of Biloma in a Dog

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Bilomas are encapsulated collections of bile outside or inside the biliary tract within the abdominal cavity. For diagnostic and therapeutic approaches, it is important to identify the origin of bile leaks from the biliary tract. This case report describes the usefulness of drip infusion cholangiography with computed tomography (DIC-CT) for detecting the site of bile leakage in a dog with biloma. A 10-year-old, castrated male Pomeranian dog was referred to our department for gastrointestinal signs. Abdominal ultrasonography detected gallbladder mucocele without evidence of defect on the wall and well-defined anechoic localized fluid accumulation around the right division of the liver. On the other hand, there was only a small amount of ascites in the abdominal cavity. The accumulated fluid collected through abdominocentesis had a bilirubin concentration of 11.4 mg/dl, which was more than twice as high as that in serum (0.4 mg/dl), but had absence of pyogenic bacteria. The DIC-CT with meglumine iotroxate showed two well-defined large fluid collections: one between right medial and lateral lobe and the other between the right lateral lobe and caudate process of caudate lobe. Three-dimensional DIC-CT views that the former was enhanced by the contrast agent and that it communicated with an intrahepatic bile duct of the right lateral lobe. Moreover, the DIC-CT images confirmed communication with each fluid collections. After 6 days of hospitalization, a decrease in the amount of accumulated fluid was confirmed, after which cholecystectomy was performed. The dog was discharged from the hospital without complications. No signs of bile leakage were observed on follow-up imaging on postoperative day 10. According to authors knowledge, this has been the first report to show that DIC-CT can be useful for determining the origin of bile leakage in dogs with bilomas.

Keywords: biloma, cholangiography, computed tomography, drip infusion, DIC-CT, dog, gallbladder mucocele

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INTRODUCTION

Bilomas are encapsulated collections of bile outside or inside biliary tract within abdominal cavity (1). In humans, bilomas were reported to be results from abdominal trauma, spontaneous leakage of the biliary tree, or iatrogenic injury (2–5). Iatrogenic damage to the biliary tract is commonly associated with laparoscopic cholecystectomy (6). Bilomas in veterinary medicine has been

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IMAGES IN SMALL ANIMAL PRACTICE

Visualising the hepatic vascular architecture using superb microvascular imaging in a dog with severe hepatic fibrosis

Superb microvascular imaging (SMI) is a novel D oppler ultrasound imaging technology using a new dutter suppression algorithm to identify and eliminate tissue movement, extract blood flow signals at a relatively high frame rate, and provide high-resolution details of vascular branches without an ultrasound contrast medium. Monochrome SMI was performed to evaluate the hepatic vascular architecture in a 9-month-old Pomeranian dog with histopathological hepatic fibrosis (Fig 1A) using an ultrasound (Aplio™ 500; Canon Medical Systems, Tochigi, Japan) and a 10-MHz linear probe (PLT-1005BT; Canon Medical Systems Corporation). The monochrome SMI was set with a low speed of 0.9 to 2.6 cm/s and a frame rate of 50 to $60\,\mathrm{f/s}$ The dog was anaesthetised and placed in a left lateral recumbent position. The hepatic parenchyma at the level of the porta hepatis was scanned in a transverse section via the intercostal approach. Monochrome SMI revealed poor ramification and tapering of the main branch of the hepatic vessels (Fig 1B). Smart three-dimensional SMI (3D-SMI), a volumerendering technology, was used to fully observe the 3D pattern visualisation of the vascular architectures. In the smart 3D-SMI mode, the transducer moves at a uniform and constant speed, and

a 3D vascular image can be reconstructed from a monochrome SM image. We also performed smart 3D -SMI in a 3-year-old healthy anaesthetised beagle dog for comparison (Supporting Information M aterial S1). Smart 3D -SMI detected severe tortuosity of the main branches and unevenness of branching in the affected dog (Fig 1C) compared with the healthy dog (Fig 1D). These remarkable vascular changes were likely caused by excessive accumulation of the extraoellular matrix in the hepatic parenchyma and the pressure of growth and expansion of regenerative nodules

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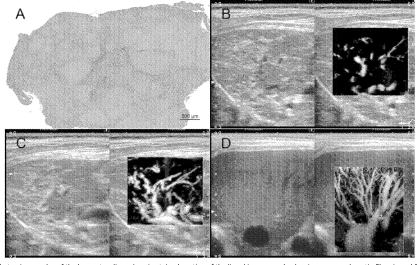


FIG 1. (A) Photomicrograph y of the haematoxylin and eosin-stained section of the liver biopsy sample showing se vere hepatic fibrosis and for mation of regenerative nodules. (B) Monochrome superb micro vascular imaging (SMI) of the hepatic parench yma of the affected dog via the right intercostal approach. Hepatic vessels show poor ramification and tapering of the main branches. (C) Smart 3D-SMI of the affected dog. Smart 3D-SMI revealed severe tortuosity of the main branches and une venness of branching. (D) Smart 3D-SMI of a healthy beagle dog. Smart 3D-SMI visualised clear ramification and tapering of the main branches without tor tuosity and evenness of branching

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講師 華園 究

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia.

<u>Hanazono K</u>, Nakamoto M, Hori A, Miyoshi K, Nakade T, Itami T, Sano T, Kato K, Ito A, Tanaka K, Yamashita K, Endoh D.

J. Vet. Med. Sci. 84:1556-1562. 2022. doi: 10.1292/jvms.22-0122.

2) Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography.

Hanazono K, Itami T, Hayasaka I, Miyoshi K, Hori A, Kato K, Endoh D. *Animals*. 12: 1175. 2022. doi: 10.3390/ani12091175.

- Ⅱ. その他<Others>
- 1) Computed angiographic variations in hepatic venous vasculature in dogs. Takagi S, Nishino A, <u>Hanazono K</u>, Hosoya K. *Vet. Surg.* 51:631-637. 2022. doi: 10.1111/vsu.13775.
- 2) Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis.

Itami T, <u>Hanazono K</u>, Makita K, Yamashita K. *J. Vet. Emerg. Crit. Care.* 32: 341-349. 2022. doi: 10.1111/vec.13178.



FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC_S/Ao) and the ratio of long to short diameter of the CVC (CVC_L/CVC_S) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC_S/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC_S/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC_S/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC_L/CVC_S of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC_S/Ao of the thorax, CVC_L/CVC_S of the thorax, CVC_S/Ao of the abdomen, and CVC_L/CVC_S of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various

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KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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最終責任者 Kiwamu Hanazono (First Author and Corresponding Author)





Article

Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

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Simple Summary: Since there is a lack of information regarding how epoprostenol, a prostacyclin, affects canine renal blood flow (RBF), we investigated the effects of short-term administration of epoprostenol at human doses of 2, 5, and 10 ng/kg/min intravenously for 20 min on RBF in six healthy dogs under anesthesia. The effects of short-term administration were investigated. As the dose of epoprostenol increased, peak systolic and end diastolic velocities of the renal arteries, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase. However, these increases were not significant. These results indicate that the administration of human doses of epoprostenol to dogs does not produce significant changes in renal or systemic circulation.

Abstract: Prostacyclin is an in vivo bioactive substance that regulates renal blood flow (RBF). Information regarding how epoprostenol, a prostacyclin preparation, affects RBF in dogs is lacking. We investigated the effects of short-term epoprostenol administration on RBF in six healthy dogs under anesthesia by administering it intravenously at human doses—2, 5, and 10 ng/kg/min for 20 min. RBF was evaluated before and during epoprostenol administration using pulsed Doppler ultrasonography, and renal perfusion was evaluated using contrast-enhanced ultrasonography. Effects on renal and systemic circulation were evaluated by measuring systolic arterial, mean arterial, diastolic arterial, pulmonary arterial, mean right atrial, and pulmonary capillary wedge pressures; heart rate; and cardiac output. Kruskal–Wallis and Bonferroni multiple comparison tests and Spearman's rank correlation coefficient were used for statistical analyses. As epoprostenol dosage increased, the peak systolic and end diastolic velocity of the renal artery, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase, although not significantly. Our results indicate that human-dose epoprostenol administration in dogs does not cause significant changes in renal or systemic circulation. However, the human doses used may have been too low to produce a clinical effect in dogs.

Keywords: anesthesia; chronic kidney disease; contrast-enhanced ultrasonography; dog; epoprostenol; prostacyclin; pulsed Doppler ultrasonography; renal circulation

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最終責任者 Kiwamu Hanazono (First Author and Corresponding Author)

ORIGINAL ARTICLE - RESEARCH

WILEY

Computed angiographic variations in hepatic venous vasculature in dogs

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Abstract

Objective: To identify the number of hepatic veins draining directly or indirectly into the caudal vena cava Thank you (CVC) using computed tomography angiography (CTA) in dogs.

Study design: Retrospective clinical study.

Animals: Client-owned dogs (n = 77).

Methods: Abdominal CTA images were analyzed. Retrospective convenience sampling was performed using archived clinical cases to determine the number of hepatic veins in each liver lobe.

Results: A median of 2 vessels from the right lateral lobe (range: 1-4) and the caudate process of the caudate lobe (range: 1-5) drained directly into the CVC. In the quadrate lobe, most common patterns consisted of 1 vessel directly draining to the CVC or indirectly via the left hepatic vein (LHV), and a vessel from quadrate lobe and right medial lobe merging into 1 vessel draining into the CVC or the LHV. A median of 3 vessels in the left lateral lobe (range: 2-8) and a median of 1 vessel in the left medial lobe (range: 1-3) drained into the LHV. In the papillary process of the caudate lobe, a median of 1 (range: 1-2) vessel drained directly into the CVC or the LHV.

Conclusion: The draining pattern of hepatic veins varied widely in all liver lobes, especially the left lateral liver lobe.

Clinical significance: Veterinary surgeons should consider the potential presence of multiple hepatic veins and their draining pattern when performing hilar liver lobe resection. Attentive evaluation of a preoperative CTA is recommended for surgical planning.

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ORIGINAL STUDY



Cardiovascular effects of intravenous pimobendan in dogs with acute respiratory acidosis

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This study was presented in part as a poster presentation at the 13th World Congress of Veterinary Anaesthesiology, Venice, Italy, September 2018.

Abstract

Objective: Acidosis decreases myocardial contractile and myofibrillar responsiveness by reducing the calcium sensitivity of contractile proteins, which could reduce the effectiveness of pimobendan. We aimed to assess the cardiovascular effects of pimobendan in dogs subjected to acute respiratory acidosis.

Design: Randomized crossover study with a 2-week washout period.

Setting: University Laboratory.

Animals: Six healthy research Beagle dogs.

Interventions: Anesthetized dogs were administered 2 doses of IV pimobendan during conditions of eucapnia (Paco₂ 35-40 mm Hg) and hypercapnia (Paco₂ 90-110 mm Hg). Eucapnia was maintained by positive pressure ventilation and hypercapnia was induced by adding exogenous CO2 to the anesthesia circuit. Heart rate (HR), systemic arterial blood pressure, cardiac output (CO), systemic and pulmonary vascular resistance (SVR and PVR, respectively), and pulmonary arterial pressure (PAP) were measured at baseline and 60 min after administering 0.125 mg/kg (low) and 0.25 mg/kg (high) pimobendan intravenously. Blood gas and biochemical analyses were performed at baseline and at the end of the experiment.

Measurements and Main Results: The median baseline blood pH was 7.41 (range: 7.33-7.45) and 7.03 (range: 6.98-7.09) under conditions of eucapnia and hypercapnia, respectively. The serum concentrations of epinephrine and norepinephrine and the HR, CO, and PAP were higher, and SVR was lower at baseline in hypercapnic dogs. Pimobendan dose-dependently increased CO in eucapnia (baseline: $3.6 \pm 0.2 \text{ L/kg/m}^2$ [mean \pm SE], low: 5.0 ± 0.4 L/kg/m², high: 5.8 ± 0.5 L/kg/m², P < 0.001) and hypercapnia (baseline: $4.9 \pm 0.5 \text{ L/kg/m}^2$, low: $5.8 \pm 0.5 \text{ L/kg/m}^2$, high: $6.2 \pm 0.5 \text{ L/kg/m}^2$, P < 0.001), and increased HR and decreased SVR and PVR under both conditions (P < 0.001). In hypercapnia, the degree of increase or decrease of these cardiovascular measurements (except for PAP) by pimobendan was less than that in the eucapnic dogs.

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食品衛生学 (Food Microbiology and Food Safety)

Akira Fukuda

Lecture

講師 福田 昭

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Infiltration of hidden antimicrobial resistance among healthy people in a Japanese community.

<u>Fukuda A</u>, Nakamura H, Umeda K, Yamamoto K, Hirai Y, Usui M, Ogasawara J. *JAC-Antimicrobial Resistance* 4:dlac031. 2022.

doi: 10.1016/j.jgar.2021.12.012

2) Conjugative IncHI2/HI2A plasmids harbouring *mcr-9* in colistin-susceptible *Escherichia coli* isolated from diseased pigs in Japan.

Fukuda A, Hitomi N, Yasuhiro S, Nakajima C, Usui M.

Access Microbiology 4:000454. 2022.

doi: 10.1016/j.vas.2022.100236

II. その他<Others>

1) Broad-host-range IncW plasmid harbouring *tet(X)* in *Escherichia coli* isolated from pigs in Japan.

Usui M, Fukuda A, Suzuki Y, Nakajima C, Tamura Y.

Journal of Global Antimicrobial Resistance in press. 97-101 2022.

doi: 10.1016/j.jgar.2021.12.012

2) Decreasing the abundance of tetracycline-resistant *Escherichia coli* in pig feces during nursery using flavophospholipol as a pig feed additive.

Kimura J, Kudo H, <u>Fukuda A</u>, Yamada M, Makita K, Oka K, Takahashi M, Tamura Y, Usui M.

Journal of Global Antimicrobial Resistance 24:220-227. 2021.

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Infiltration of hidden antimicrobial resistance among healthy people in a Japanese community

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Background: Under non-antimicrobial selective pressure, antimicrobial-resistant bacteria do not easily become dominant in the microbiota. Furthermore, their low levels prevent detection by isolation, resulting in an underestimation of the prevalence of antimicrobial-resistant bacteria.

Objectives: We evaluated the infiltration of antimicrobial-resistant bacteria and their related β -lactamase genes among healthy people in non-clinical settings.

Methods: Cephalosporin- and fluoroquinolone-resistant *Escherichia coli* and *bla* genes were quantified in 217 faecal samples from healthy people in non-clinical settings in Japan. *E. coli* colonies grown on deoxycholate hydrogen sulphide-lactose (DHL) agar, with and without antimicrobials (cefotaxime and ciprofloxacin), were quantified, and *E. coli* isolates were analysed for their susceptibility to antimicrobials and the presence of *bla* genes. DNA extracted from faecal samples was used to quantify *bla* genes using quantitative PCR (qPCR).

Results: The isolation rates of cefotaxime- and ciprofloxacin-resistant *E. coli* were 6.9% and 12.4%, respectively, using agars without antimicrobials, and 12.0% and 24.4%, respectively, using agars with antimicrobials. For samples from which cefotaxime- and ciprofloxacin-resistant *E. coli* were isolated only using agars with antimicrobials, the ratios of cfu on DHL agars with and without antimicrobials were below —2 log. *E. coli* harbouring *bla* genes were isolated from 35.0% of the faecal samples using agars, and *bla* genes were detected in 65.0% of faecal DNA samples using qPCR.

Conclusions: Among people carrying cefotaxime- and ciprofloxacin-resistant *E. coli* in non-clinical settings, cefotaxime- and ciprofloxacin-resistant *E. coli* were not dominant in half of the subjects. These individuals may play a role as reservoirs of antimicrobial-resistant bacteria.

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SHORT COMMUNICATION

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@ACCESS

Conjugative IncHI2/HI2A plasmids harbouring mcr-9 in colistinsusceptible Escherichia coli isolated from diseased pigs in Japan

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Abstract

Colistin is a last resort antimicrobial used for the treatment of gram-negative bacterial infections. Plasmid-mediated colistin resistance (mcr) genes are a cause of global concern, and, thus far, mcr-1-10 have been identified. In a previous study, we screened mcr-1-6 in Escherichia coli derived from diseased pigs in Japan and reported a high prevalence of mcr-1, -3 and -5. However, the previous report on the prevalence of mcr genes was inaccurate. In the present study, we aimed to clarify the prevalence of all reported variants of mcr in E. coli derived from the diseased pigs, which were previously screened for mcr-1-5. Additionally, we also characterized the mcr-9-positive E. coli, which was detected in this study. We screened mcr in 120 E. coli strains from diseased pigs and mcr-positive E. coli and an mcr-carrying plasmid were also characterized. One mcr-9-positive colistin-susceptible E. coli strain was detected (0.8%). Plasmid-mediated mcr-9 was transferred to E. coli ML4909 as the recipient strain, and it was located on IncH12/H12A plasmid p387_L with other antimicrobial resistance genes (ARGs). The region harbouring ARGs including mcr-9, was similar to that on the Klebsiella pneumoniae chromosome harbouring mcr-9 isolated in Japan. mcr-3, -5 and -9 were detected (4.2%) in colistin-susceptible strains. mcr-9 was found to be disseminated via the plasmid IncH12/H12A p387_L and transferred and inserted into chromosomes via a transposon. Our results suggest that mcr genes should be monitored regularly, regardless of their susceptibility to colistin.

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Journal of Global Antimicrobial Resistance





Broad-host-range IncW plasmid harbouring *tet*(X) in *Escherichia coli* isolated from pigs in Japan



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ABSTRACT

Objectives: Tetracyclines are used in veterinary medicine for livestock. Tigecycline, a semisynthetic tetracycline derivative, is a last-resort antimicrobial used to treat multidrug-resistant Gram-negative bacterial infections. The prevalence of variants of the mobile tigecycline resistance gene tet(X) in livestock is increasing worldwide. However, the prevalence of Tet(X) among livestock in Japan is unclear. This study was conducted to clarify the prevalence of Tet(X) in pigs in Japan, focusing on isolation and molecular characterisation of plasmid-mediated tet(X)-positive Escherichia coli through retrospective analysis.

Methods: We retrospectively screened for tigecycline-resistant E. coli strains isolated from pigs. The tigecycline-resistant strain and tet(X)-harbouring plasmid were characterised.

Results: The IncW plasmid harbouring the tet(X) variant [previously named as tet(X6)] was detected in one E. coli isolate from pigs (0.8%; 1/120) in 2012. The tet(X) plasmid was transferable by conjugation to the E. coli ML4909 recipient strain. Some mobile genetic elements (TnAs3 and ISVsa3) were observed in the region surrounding tet(X). The tet(X)-harbouring plasmid shared a conserved backbone with IncW plasmid R388, which is a broad-host-range plasmid.

Conclusion: The emergence and spread of tet(X) variants in Enterobacterales poses a public-health concern. To the best of our knowledge, this is the first report of the emergence of an IncW plasmid harbouring tet(X). Using tetracyclines in livestock exerts selective pressure on the tet(X) plasmid; therefore, prudent use of tetracyclines is required.

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Decreased colistin resistance and *mcr-1* prevalence in pig-derived *Escherichia coli* in Japan after banning colistin as a feed additive



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7.

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ABSTRACT

Background: Antimicrobial resistance to colistin, a widely used feed additive for farm animals across the world, has raised public health concern in recent years. Since July 2018, its use as feed additive has been banned in Japan to reduce the spread of plasmid-based mobilized colistin resistance (mcr) genes and the subsequent development of colistin-resistant bacteria. Evaluating the effects of these measures is required.

Methods: We evaluated the effects of colistin use, as a feed additive, on colistin resistance in pigs (n=5) from birth to finishing in the farm. Moreover, to evaluate changes in colistin resistance and mcr gene prevalence in response to colistin withdrawal, E. coli samples derived from pig faeces sourced from the fields of three geographically distinct farms were characterized before and after the withdrawal of colistin as a feed additive.

Results: Colistin-resistant Escherichia coli in pigs (n=5) increased during the colistin administration period and decreased immediately after its end. In three fields, the colistin resistance rate and prevalence of mcr-1 decreased immediately and significantly after the ban. However, colistin-resistant and mcr-1-positive E. coli were still detected in all three farm fields 12 months after the ban on colistin use. Conclusion: Agricultural colistin use caused selective pressure that contributed to widespread mcr dissemination in Japan. Colistin resistance and the presence of mcr genes should be continuously monitored in food-producing animals.

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Jumpei Fujiki

Lecturer

講師 藤木 純平

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Biological properties of Staphylococcus virus ΦSA012 for phage therapy. **Fujiki J**, Nakamura T, Nakamura K, Nishida K, Amano Y, Watanabe Y, Gondaira S, Usui M, Shimizu M, Miyanaga K, Watanabe S, Iwasaki T, Kiga K, Hanawa T, Higuchi H, Sawa T, Tanji Y, Tamura Y, Cui L, Iwano H. *Sci Rep.* 2022 Dec 9;12(1):21297. doi: 10.1038/s41598-022-25352-6.
- 2) Bisphenol A-sulfate conjugate disrupts AURKA transcription and cell cycle in BeWo cytotrophoblasts.

<u>Fujiki J</u>, Uchida M, Tsunoda S, Maeda N, Inoue H, Yokota H, Iwano H. *Mol Cell Endocrinol.* 2022 Apr 5;545:111561. doi: 10.1016/j.mce.2022.111561.

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Iwano H.

 Whole-Genome Sequencing of Pasteurella multocida Strain Pm1, Isolated from a Calf. Gondaira S, <u>Fujiki J</u>, Hirano Y, Murata R, Uchida I, Usui M, Iwasaki T, Okabayashi T, Iwano H, Higuchi H.

Microbiol Resour Announc. 2022 Apr 21;11(4):e0004222. doi: 10.1128/mra.00042-22.

- Relationship between Escherichia coli virulence factors, notably kpsMTII, and symptoms of clinical metritis and endometritis in dairy cows.
 Yamamura F, Sugiura T, Munby M, Shiokura Y, Murata R, Nakamura T, <u>Fujiki J</u>,
 - J Vet Med Sci. 2022 Mar 15;84(3):420-428. doi: 10.1292/jvms.21-0586.
- 3) Testicular induced corticosterone synthesis in male rats under fasting stress. Maeda N, **Fujiki J**, Hasegawa Y, Ieko T, Miyasho T, Iwasaki T, Yokota H. *Steroids*. 2022 Jan;177:108947. doi: 10.1016/j.steroids.2021.108947.

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OPEN Biological properties of *Staphylococcus* virus ΦSA012 for phage therapy

Jumpei Fujiki¹, Tomohiro Nakamura^{1,2,3}, Keisuke Nakamura¹, Keita Nishida¹, Yurika Amano¹, Yusaku Watanabe¹, Satoshi Gondaira¹, Masaru Usui⁵, Masaru Shimizu⁶, Kazuhiko Miyanaga², Shinya Watanabe², Tomohito Iwasaki⁸, Kotaro Kiga^{3,2}, Tomoko Hanawa⁹, Hidetoshi Higuchi¹, Teiji Sawa⁶, Yasunori Tanji², Yutaka Tamura⁵, Longzhu Cui⁷ & Hidetomo Iwano^{1,23}

Staphylococcus virus ФSA012 has a wide host range and efficient lytic activity. Here, we assessed the biological stability of ФSA012 against temperature, freeze-thawing, and pH to clinically apply the phage. In addition, inoculation of ФSA012 through i.p. and i.v. injections into mice revealed that phages were reached the limit of detection in serum and accumulated notably spleens without inflammation at 48 h post-inoculation. Furthermore, inoculation of ФSA012 through s.c. injections in mice significantly induced IgG, which possesses neutralizing activity against ФSA012 and other Staphylococcus viruses, ФSA039 and ФMR003, but not Pseudomonas viruses ФS12-3 and ФR18 or Escherichia viruses T1, T4, and T7 in vitro. Immunoelectron microscopic analysis showed that purified anti-phage IgG recognizes the long-tail fiber of staphylococcus viruses. Although S. aureus inoculation resulted in a 25% survival rate in a mouse i.p. model, ФSA012 inoculation (i.p.) improved the survival rate to 75%; however, the survival rate of ФSA012-immunized mice decreased to less than non-immunized mice with phage i.v. injection at a MOI of 100. These results indicated that ФSA012 possesses promise for use against staphylococcal infections but we should carefully address the appropriate dose and periods of phage administration. Our findings facilitate understandings of staphylococcus viruses for phage therapy.

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最終責任者 Hidetomo Iwano (Corresponding Author)



Molecular and Cellular Endocrinology







Bisphenol A-sulfate conjugate disrupts AURKA transcription and cell cycle in BeWo cytotrophoblasts

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ARTICLE INFO

Keywords Placenta Sisphenol BPA

Endocrine-disrupting chemicals (EDCs) Sulfate-sulfatase pathway

ABSTRACT

Bisphenol A (BPA) has been shown to exhibit various toxic effects, including the induction of reproductive disorders. Generally, BPA is converted to conjugated metabolites, leading to bio-inactivation. On the other hand, the toxicity of conjugated metabolites is not fully understood. Notably, the placenta develops the sulfate-sulfatase pathway, which transports and reactivates sulfated steroids. Therefore, we investigated the potential adverse effects of the BPA-sulfate conjugate (BPA-S) on human placenta-derived BeWo cytotrophoblasts. In the present study, high-concentration BPA-S (100 µM) induced significant inhibition of BeWo growth, with effects similar to those seen with unconjugated BPA (100 µM and 100 nM). This growth inhibition was restored by treatment of the cells with an inhibitor of the organic anion-transporting peptides (OATPs) (bromosulphophthalein) or with a sulfatase (STS) inhibitor (STX64). BeWo exhibits expression of the genes encoding OATP1A2 and OATP4A1 as known sulfated steroid transporters and STS, suggesting that BPA-S suppresses cell growth activity via the sulfate-sulfatase pathway. In addition, cell cycle analysis revealed that BPA-S (100 µM) increased the fraction of cytotrophoblasts in the G2/M phases and significantly decreased the accumulation of the transcript encoding Aurora kinase A (AURKA), which is a critical regulator of cellular division. These results suggested that BPA-S triggers cell cycle arrest and inhibits proliferation of BeWo cytotrophoblasts by decreased AURKA, an effect that is mediated by the sulfate-sulfatase pathway. Overall, these findings provide insights into the reactivation of sulfated endocrine-disrupting chemicals and subsequent adverse effects.

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Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

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ABSTRACT Bovine pneumonia is a disease that causes significant economic losses in livestock industries and is vital for animal welfare. The whole-genome sequence of *Pasteurella multocida* strain Pm1, isolated from a calf suffering from pneumonia in Japan, is reported here.

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FULL PAPER

Theriogenology

Relationship between *Escherichia coli* virulence factors, notably *kpsMTII*, and symptoms of clinical metritis and endometritis in dairy cows

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ABSTRACT. Although Escherichia coll is a commensal bacterium of the bovine vaginal microbiota, it is an important pathogenic bacterium that causes diseases of the reproductive tract and subfertility. Recent studies have focused on virulence factors (VFs) of intrauterine £. coli; however, actual endometrial VFs have not been clearly identified. The purpose of this study was to identify the VFs of E. coli associated with clinical metritis and endometritis. Thirty-two strains of E. coli and four mixed Trueperella pyogenes (TP) strains were detected in the uterus of 19 Holstein dairy cows with obvious clinical signs (between 8 and 66 days postpartum). The presence of six E. coli VFs (fimH, fyuA, kpsMTli, hra1, csgA, and astA) was examined by PCR, and clinical signs and reproductive performance (mixed TP, the percentage of polymorphonuclear neutrophils [PMN%], days to uterine involution, etc.) were evaluated. Four VFs (fimH, hra1, csqA, and astA) were detected in all E. coli strains, whereas fyuA and kpsMTII were detected in 94% and 50% of strains, respectively. Cows with E. coli strains harboring kpsMTII exhibited significantly severe clinical scores (vaginal discharge score, PMN%, uterine involution), suggesting that kpsMTli is a key VF for progression of clinical metritis and endometritis. In the present study, we clearly identified six VFs associated with clinical metritis and endometritis. In addition, E. coli strains with kpsM7li probably play a crucial role in the progression of clinical metritis and endometritis.

KEY WORDS: Escherichia coli, kpsMTII, postpartum uterine disease, uterine restoration time, virulence factor

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Steroids



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Testicular induced corticosterone synthesis in male rats under fasting stress

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ARTICLE INFO

Keywords: Testicular steroidogenesis Testosterone Corticosterone 39-hydroxysteroid dehydrogenase Facting stress

ABSTRACT

Testicular steroidogenesis is depressed by adrenal-secreted corticosterone (CORT) under stress. However, the mechanisms are not well understood. This study investigated the details of testicular steroidogenesis depression during fasting. Blood levels of adrenocorticotropic hormone secreted from the pituitary glands increased, but blood CORT was not changed in rats that fasted for 96 h, in spite of the rats being severely stressed. CORT in fasting adult male rats increased more than three times in the testis, but reduced testicular testosterone (T) and blood T levels to 5% and 2% of the control, respectively, was observed. The contents of T precursor (except PGN) were drastically reduced in the fasted-rat testes. Testicular CORT levels were elevated, but the enzymatic activity of cytochrome P45011β, which produces CORT, remained unchanged. The enzymatic activities of 3β-hydroxysteroid dehydrogenase (3β-HSD), mediating the conversion of pregnenolone to progesterone, decreased in the fasted-rat testes. Thus, fasting suppressed testicular steroidogenesis by affecting the enzyme activity of 3β-HSD in the testes and drastically reduced T and increased CORT synthesis. It can be considered that T synthesis involved in cell proliferation is suppressed due to lack of energy during fasting. Conversely, 11β-hydroxylase enzyme activity was induced and CORT synthesis is increased to cope with the fasting stress. Hence, it can be concluded that CORT synthesis in the testes plays a role in the local defense response.

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 - Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

Hanazono K, Itami T, Hayasaka I, <u>Miyoshi K</u>, Hori A, Kato K, Endoh D. *Animals (Basel)* 4;12(9):1175. doi: 10.3390/ani12091175

2) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia.

Hanazono K, Nakamoto M, Hori A, <u>Miyoshi K</u>, Nakade T, Itami T, Sano T, Kato K, Ito A, Tanaka K, Yamashita K, Endoh D.

J Vet Med Sci. 84(12): 1556–1562. doi: 10.1292/jvms.22-0122

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Article

Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

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Simple Summary: Since there is a lack of information regarding how epoprostenol, a prostacyclin, affects canine renal blood flow (RBF), we investigated the effects of short-term administration of epoprostenol at human doses of 2, 5, and 10 ng/kg/min intravenously for 20 min on RBF in six healthy dogs under anesthesia. The effects of short-term administration were investigated. As the dose of epoprostenol increased, peak systolic and end diastolic velocities of the renal arteries, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase. However, these increases were not significant. These results indicate that the administration of human doses of epoprostenol to dogs does not produce significant changes in renal or systemic circulation.

Abstract: Prostacyclin is an in vivo bioactive substance that regulates renal blood flow (RBF). Information regarding how epoprostenol, a prostacyclin preparation, affects RBF in dogs is lacking. We investigated the effects of short-term epoprostenol administration on RBF in six healthy dogs under anesthesia by administering it intravenously at human doses—2, 5, and 10 ng/kg/min for 20 min. RBF was evaluated before and during epoprostenol administration using pulsed Doppler ultrasonography, and renal perfusion was evaluated using contrast-enhanced ultrasonography. Effects on renal and systemic circulation were evaluated by measuring systolic arterial, mean arterial, diastolic arterial, pulmonary arterial, mean right atrial, and pulmonary capillary wedge pressures; heart rate; and cardiac output. Kruskal–Wallis and Bonferroni multiple comparison tests and Spearman's rank correlation coefficient were used for statistical analyses. As epoprostenol dosage increased, the peak systolic and end diastolic velocity of the renal artery, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase, although not significantly. Our results indicate that human-dose epoprostenol administration in dogs does not cause significant changes in renal or systemic circulation. However, the human doses used may have been too low to produce a clinical effect in dogs.

Keywords: anesthesia; chronic kidney disease; contrast-enhanced ultrasonography; dog; epoprostenol; prostacyclin; pulsed Doppler ultrasonography; renal circulation



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FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC (CVC₅/Nc) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₅/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₅/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC₅/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/CVC₅ of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₅/Ao of the thorax, CVC₁/CVC₅ of the thorax, CVC₅/Ao of the abdomen, and CVC₁/CVC₅ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

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KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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 - 1) Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf. Gondaira S, Fujiki J, Hirano Y, <u>Murata R</u>, Uchida I, Usui M, Iwasaki T, Okabayashi T, Iwano H, Higuchi H.
 - Microbiol. Resour. Announc. 11: e0004222. 2022. doi: 10.1128/mra.00042-22.
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 - J. Vet. Med. Sci. 84: 420-428. 2022. doi: 10.1292/jvms.21-0586.
- 3) Intra-macrophage expression of ArtAB toxin gene in *Salmonella*.

 Miura S, Satoh R, Tamamura-Andoh Y, Tokugawa K, Beppu M, Nozaki C, <u>Murata R</u>, Kusumoto M, Uchida I.
 - Microbiology 168: 001152. 2022. doi: 10.1099/mic.0.001152.







Whole-Genome Sequencing of *Pasteurella multocida* Strain Pm1, Isolated from a Calf

Satoshi Gondaira,^a Jumpei Fujiki,^b Yuki Hirano,^c Ryo Murata,^d Ikuo Uchida,^d Masaru Usui,^e Tomohito Iwasaki,^f Tamaki Okabayashi,^g Hidetomo Iwano,^b Hidetoshi Higuchi^a

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FULL PAPER

Theriogenology

Relationship between *Escherichia coli* virulence factors, notably *kpsMTII*, and symptoms of clinical metritis and endometritis in dairy cows

Fuminosuke YAMAMURA¹⁾, Tomochika SUGIURA²⁾, Montgomery MUNBY¹⁾, Yusei SHIOKURA¹⁾, Ryo MURATA³⁾, Tomohiro NAKAMURA¹⁾, Jumpei FUJIKI¹⁾ and Hidetomo IWANO¹⁾*

ABSTRACT. Although Escherichia coli is a commensal bacterium of the bovine vaginal microbiota, it is an important pathogenic bacterium that causes diseases of the reproductive tract and subfertility. Recent studies have focused on virulence factors (VFs) of intrauterine E. coli; however, actual endometrial VFs have not been clearly identified. The purpose of this study was to identify the VFs of E. coli associated with clinical metritis and endometritis. Thirty-two strains of E. coli and four mixed Trueperella pyogenes (TP) strains were detected in the uterus of 19 Holstein dairy cows with obvious clinical signs (between 8 and 66 days postpartum). The presence of six E. coli VFs (fimH, fyuA, kpsMTII, hra1, csgA, and astA) was examined by PCR, and clinical signs and reproductive performance (mixed TP, the percentage of polymorphonuclear neutrophils [PMN%], days to uterine involution, etc.) were evaluated. Four VFs (fimH, hra1, csgA, and astA) were detected in all E. coli strains, whereas fyuA and kpsMTII were detected in 94% and 50% of strains, respectively. Cows with E. coli strains harboring kpsMTII exhibited significantly severe clinical scores (vaginal discharge score, PMN%, uterine involution), suggesting that kpsMTII is a key VF for progression of clinical metritis and endometritis. In the present study, we clearly identified six VFs associated with clinical metritis and endometritis. In addition, E. coli strains with kpsMTII probably play a crucial role in the progression of clinical metritis and endometritis.

KEY WORDS: Escherichia coli, kpsMTII, postpartum uterine disease, uterine restoration time, virulence factor

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RESEARCH ARTICLE

MICROBIOLOGY SOCIETY

Miura et al., Microbiology 2022;168:001152 DOI 10.1099/mic.0.001152

Intra-macrophage expression of ArtAB toxin gene in Salmonella

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Abstract

Salmonella enterica subspecies enterica serovar Typhimurium (S. Typhimurium) definitive phage type 104 (DT104), S. Worthington, and S. bongori produce ArtAB toxin, which catalyses ADP-ribosylation of pertussis toxin-sensitive G protein. ArtAB gene (artAB) is encoded on a prophage in Salmonella, and prophage induction by SOS-inducing agents is associated with increases in ArtAB production in vitro. However, little is known about the expression of artAB in vivo. Here, we showed a significant increase in artAB transcription of DT104 within macrophage-like RAW264.7 cells. Intracellular expression of ArtAB was also observed by immunofluorescence staining. The induced expression of artAB in DT104 and S. bongori was enhanced by treatment of RAW264.7 cells with phorbol 12-myristate 13-acetate (PMA), which stimulates the production of reactive oxygen species (ROS); however, such induction was not observed in S. Worthington. Upregulation of oxyR, a major regulator of oxidative stress, and cl, a repressor of prophage induction, was observed in S. Worthington within RAW264.7 cells treated with PMA but not in the DT104 strain. Although the expression of oxyR was increased, artAB was upregulated in S. bongori, which lacks the cl gene in the incomplete artAB-encoded prophage. Taken together, oxidative stress plays a role in the production of artAB toxins in macrophages, and high expression levels of oxyR and cl are responsible for the low expression of artAB. Therefore, strain variation in the level of artAB expression within macrophages could be explained by differences in the oxidative stress response of bacteria and might be reflected in its virulence.

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 - 1) Near-infrared photoimmunotherapy induced tumor cell death enhances tumor dendritic cell migration.

Moriya T, Hashimoto M, Matsushita H, Masuyama S, Yoshida R, Okada R, Furusawa A, Fujimura D, Wakiyama H, Kato T, Choyke PL, Kusumoto Y, Chtanova T, Kobayashi H, Tomura M.

Cancer Immunol Immunother 71(12):3099-3106. 2022 doi: 10.1007/s00262-022-03216-2.

II. その他<Others>

RESEARCH REPORT



Near-infrared photoimmunotherapy induced tumor cell death enhances tumor dendritic cell migration

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Abstract

Near-infrared photoimmunotherapy (NIR-PIT) selectively kills tumor cells to which the photo-absorber dye IR700DX-conjugated antibodies are bound and induces a systemic anti-tumor immune response. NIR-PIT induces immunogenic cell death (ICD), releases damage-associated molecular patterns (DAMPs) molecules from dying tumor cells, and activates dendritic cells (DCs). However, it is unclear whether NIR-PIT affects migration of tumor-infiltrating (Ti)-DCs to draining lymph nodes (dLNs), where a systemic anti-tumor response is induced. Here, we utilized in vivo photolabeling of Ti-DCs in tumors in photoconvertible protein Kikume Green-Red (KikGR) mice to show that NIR-PIT enhanced migration of Ti-DCs including cDC1s, cDC2s, and CD326⁺ DCs to dLNs. This effect was abolished by blocking adenosine triphosphate (ATP), one of the DAMPs molecules, as well as by inhibition of Gai signaling by pertussis toxin. Thus, ICD induction by NIR-PIT stimulates Ti-DC migration to dLNs via ATP-P2X7 receptor and Gai protein-coupled receptor signaling pathways and may augment tumor antigen presentation to induce anti-tumor T cells in dLNs.

Keywords Near-infrared photoimmunotherapy · Immunogenic cell death · Tumor-infiltrating dendritic cells · Tumor · Cellular migration · Photo labeling

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- I. 筆頭または責任著者 <First or Corresponding Author>
- II. その他<Others>
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Article

Cloning, Expression and Evaluation of Thioredoxin Peroxidase-1 Antigen for the Serological Diagnosis of Schistosoma mekongi Human Infection

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Abstract: Schistosoma mekongi, a blood fluke that causes Asian zoonotic schistosomiasis, is distributed in communities along the Mekong River in Cambodia and Lao People's Democratic Republic. Decades of employing numerous control measures including mass drug administration using praziquantel have resulted in a decline in the prevalence of schistosomiasis mekongi. This, however, led to a decrease in sensitivity of Kato–Katz stool microscopy considered as the gold standard in diagnosis. In order to develop a serological assay with high sensitivity and specificity which can replace Kato–Katz, recombinant S. mekongi thioredoxin peroxidase-1 protein (rSmekTPx-1) was expressed and produced. Diagnostic performance of the rSmekTPx-1 antigen through ELISA for detecting human schistosomiasis was compared with that of recombinant protein of S. japonicum TPx-1 (rSjTPx-1) using serum samples collected from endemic foci in Cambodia. The sensitivity and specificity of rSmekTPx-1 in ELISA were 89.3% and 93.3%, respectively, while those of rSjTPx-1 were 71.4% and 66.7%, respectively. In addition, a higher Kappa value of 0.82 calculated between rSmekTPx-1 antigen ELISA and Kato–Katz confirmed better agreement than between rSjTPx-1 antigen ELISA and Kato–Katz (Kappa value 0.38). These results suggest that ELISA with rSmekTPx-1 antigen can be a potential diagnostic method for detecting active human S. mekongi infection.

Keywords: Schistosoma mekongi; Schistosoma japonicum; recombinant antigen; ELISA



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ORIGINAL ARTICLE



Comparative mitogenomics elucidates the population genetic structure of *Amblyomma testudinarium* in Japan and a closely related *Amblyomma* species in Myanmar

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Abstract

Ticks are the second most important vector capable of transmitting diseases affecting the health of both humans and animals. Amblyomma testudinarium Koch 1844 (Acari: Ixodidae), is a hard tick species having a wide geographic distribution in Asia. In this study, we analyzed the composition of A. testudinarium whole mitogenomes from various geographical regions in Japan and investigated the population structure, demographic patterns, and phylogeographic relationship with other ixodid species. In addition, we characterized a potentially novel tick species closely related to A. testudinarium from Myanmar. Phylogeographic inference and evolutionary dynamics based on the 15 mitochondrial coding genes supported that A. testudinarium population in Japan is resolved into a star-like haplogroup and suggested a distinct population structure of A. testudinarium from Amami island in Kyushu region. Correlation analysis using Mantel test statistics showed that no significant correlation was observed between

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Parasitology International





Resolution of cryptic species complexes within the genus *Metagonimus* (Trematoda: Heterophyidae) in Japan, with descriptions of four new species

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ARTICLEINFO

Keywords: Metagonimus Japan Cryptic species complex New species Fish second intermediate hosts

ABSTRACT

A nationwide fish survey was conducted in Japan to detect metacercariae of the genus Metagonimus (Trematoda: Heterophyidae). The metacercariae were subjected to DNA barcoding for molecular species identification. A phylogeny inferred from the sequences of mitochondrial cytochrome c oxidase subunit 1 (cox1) prompted us to recognize three cryptic species complexes (i.e., the M. miyatai complex, the M. takahashii complex, and the M. katsuradai complex). Each complex included one or two undescribed species. For morphological description, adult flukes of each species were raised through the experimental infections of immunosuppressed mice. We propose M. saitoi n. sp., M. kogai n. sp., M. shimazui n. sp., and M. kinoi n. sp., based on their phylogeny, morphology, biogeography, and ecology (host-parasite relationships). The originally described species, M. miyatai, was split into M. miyatai sensu stricto and M. saitoi n. sp. The former is distributed mainly in eastern Japan and uses the sweetfish (Plecoglossus altivelis) and daces (Pseudaspius hakonensis and Ps. sachalinensis) as principal second intermediate hosts, while the latter is in western Japan and its principal fish hosts are the dark chub (Nipponocypris temminckii) and the pale chub (Opsariichthys platypus). The present survey resolves a long-standing controversy on the microtaxonomy of Metagonimus in Japan since the first discovery of Metagonimus yokogawai in 1912, and shows that 10 species of Metagonimus are still distributed in Japan, although human metagonimissis is almost eradicated.

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Genotyping; Malawi; population structure; Theileria parva

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Genotyping of *Theileria parva* populations in vaccinated and non-vaccinated cattle in Malawi

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Abstract

Theileria parva is an apicomplexan protozoan parasite that causes bovine theileriosis (East Coast Fever; ECF) in central, eastern and southern Africa. In Malawi, ECF is endemic in the northern and central regions where it has negatively affected the development of dairy industry. Despite its endemic status the genetic population structure of T. parva in Malawi is currently unknown. To obtain an understanding of T. parva in Malawi, we performed population genetics analysis of T. parva populations in cattle vaccinated with the Muguga cocktail live vaccine and non-vaccinated cattle using mini- and microsatellite markers covering all the four T. parva chromosomes. The T. parva Muguga strain was included in this study as a reference strain. Linkage disequilibrium was observed when all samples were treated as a single population. There was sub-structuring among the samples as shown by the principal coordinate analysis. Majority of the samples clustered with the T. parva Muguga reference strain suggesting that the isolates in Malawi are closely related to the vaccine component, which support the current use of Muguga cocktail vaccine to control ECF. The dustering of samples from non-endemic southern region with those from endemic central region suggests expansion of the distribution of T. parva in Malawi.

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Parasitology International





Molecular analyses confirm the coexistence of Fasciola gigantica and parthenogenetic Fasciola in the Philippines

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ARTICLE INFO

Keywords: Fasciola gigantica Parthenogenetic Fasciola Philippines Pepck ND1

ABSTRACT

Fasciola flukes collected from domestic buffalos and cattle in the Philippines were confirmed as Fasciola gigantica and parthenogenetic Fasciola based on DNA analyses of nuclear pepck and pold genes, and the mitochondrial ND1 gene. This study is the first to elucidate that F. gigantica and parthenogenetic Fasciola coexist in the Philippines with prevalences of 90.6% and 9.4%, respectively. The F. gigantica population showed a high genetic diversity with 25 ND1 haplotypes, suggesting that F. gigantica has existed in the Philippines for a long time. In contrast, parthenogenetic Fasciola flukes showed a single ND1 haplotype (Fsp-ND1-P1), which was identical to the founder haplotype, Fg-C2 of parthenogenetic Fasciola in China. These results indicate that parthenogenetic Fasciola in the Philippines is a recently introduced population from a neighboring continent.

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The causative agents of fascioliasis in animals and humans: Parthenogenetic *Fasciola* in Asia and other regions

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Keywords:
Parthenogenetic Pasciola
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ABSTRACT

Parthenogenetic Fasciola is the causative agent of fascioliasis in animals and humans and is widely distributed in Asian countries, such as Japan, South Korea, China, Vietnam, Thailand, the Philippines, Myanmar, Bangladesh, Nepal, and India. Parthenogenetic Fasciola geographically originated from central and eastern China, where it exists between the habitats of Fasciola hepatica and Fasciola gigantica; it likely appeared thousands of years ago following hybridization between F. hepatica and F. gigantica. Parthenogenetic Fasciola consists of diploids and $triploids\ that\ possess\ nuclear\ genome\ of\ both\ \emph{F.}\ \textit{hepatica}\ and\ \emph{F.}\ \textit{gigantica}\ and\ mitochondrial\ genome\ of\ either$ F. hepatica or F. gigantica. Maternal parents of parthenogenetic Fasciola are either F. hepatica having Fh-C4 haplotype or F. gigantica having Fg-C2 haplotype in mitochondrial NADH dehydrogenase subunit 1 (ND1) nucleotide sequences. Parthenogenetic Fasciola flukes with the Fh-C4 haplotype have spread from China to South Korea and Japan, whereas the flukes with the Fg-C2 haplotype have not only spread to Korea and Japan but also southward to Vietnam, Thailand, the Philippines, Myanmar, Bangladesh, Nepal, and India. Parthenogenetic Fasciola can be distinguished from F. hepatica and F. gigantica using combinational DNA sequence analysis of nuclear phosphoenolpyruvate carboxykinase (pepck) and DNA polymerase delta (pold) along with mitochondrial ND1 markers. The establishment of parthenogenetic Fasciola is expected as follows: parthenogenetic diploids with the Fh-C4 and Fg-C2 haplotypes first appeared based on single or multiple interspecific hybridization events; subsequently, parthenogenetic triploids emerged via backcross events between the maternal parthenogenetic diploid and either paternal bisexual F. hepatica or F. gigantica. Parthenogenetic Fasciola diploids and triploids then survived for thousands of years by clonal parthenogenetic reproduction, and generated descendants with ND1 haplotypes, which were derived from the Fh-C4 and Fg-C2 due to nucleotide substitution. Thus, the emergence of parthenogenetic Fasciola may be due to extremely uncommon and accidental events. Parthenogenetic Fasciola should be treated as a new asexual hybrid species.

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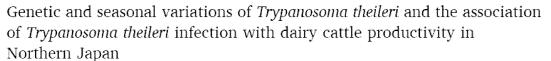
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Research paper





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ARTICLE INFO

Keywords: Genotyping Metabolic profile test Milk Mixed model Seasonal variations Trypanosoma theileri

ABSTRACT

Trypanosoma thelleri is considered a non- or low-pathogenic trypanosome that generally causes latent infection in apparently healthy cattle; however, T. theileri propagates in the bloodstream and may cause clinical disease in pregnant animals or co-infection with bovine leukemia virus or Theileria orientalis. In the current study, a monthly survey of T. theileri infection over one year was carried out in a research dairy farm in Hokkaido, Japan to determine the 1) seasonal variations in the prevalence, 2) genetic characterization of T. theileri, and 3) associations of milk and blood parameters in dairy cattle with T. theileri infection, including data of metabolic profile tests and dairy herd performance tests, using linear mixed models. We found that 1) the prevalence of T. thelleri infection was significantly higher in summer and winter than in other seasons; 2) T. thelleri possibly showed genetic diversity in Eastern Hokkaido; and 3) T. thelleri infection was associated with significantly lower levels of blood urea nitrogen, milk protein, and solids-not-fat, which are caused by a low rumen fermentation level. This is the first study to report the negative impact of T. theileri infection in dairy cattle, and our study indicates that control of T. theileri infection can improve the productivity of dairy cattle.

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Brachylaima phaedusae n. sp. (Trematoda: Brachylaimidae) from door snails in Japan

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ARTICLEINFO

Keywords: Brachylaima phaedusae n. sp. Door snails Japan

ABSTRACT

The metacercarial infections of door snails (Gastropoda: Clausillidae) with unknown species of the genus Brachylaima (Trematoda: Brachylaimidae) have recently been reported in eastern Honshu and Kyushu, Japan. A large scale snail survey was carried out to clarify their taxonomic status. From the period of 2015 to 2020, a total of 1239 land snails (768 door snails and 471 others) were collected from 32 localities in Honshu, Shikoku, and Kyushu. The resulting trematode isolates were identified as Brachylaima sp. by mitochondrial DNA barcoding. The sporocysts were found only a few from Megalophaedusa sublumellata (Clausiliidae), Tauphaedusa subaculus (Clausiliidae), and Acgista trochula (Camaenidae), while the metacercariae were frequently detected from 14 species of Clausiliidae and 2 species of other families. Although Brachylaima sp. showed a broad range of intermediate hosts, door snails seem to be very important to drive the life cycle. The gravid adults of Brachylaima sp. was experimentally raised from metacercariae using immunosuppressed mice. Morphological, phylogenetical, and ecological considerations prompted us to propose Brachylaima phaedusae n. sp. for this unknown species. The definitive hosts of the new species are completely unknown. The wide geographic distribution and high genetic diversity of the new species suggest a possibility that the definitive host is ground-foraging birds, which prefer door snails.

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- II. その他<Others>
 - 1) Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs.
 - Chen IY, Tamogi H, Wei Y, <u>Kato K</u>, Itami T, Sano T, Yamashita K. *Vet Anaesth Analg.* 49:36-44. 2022. doi: 10.1016/j.vaa.2021.10.002.
 - 2) Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits.
 - Wei Y, Hori A, Chen IY, Tamogi H, Hirokawa T, **Kato K**, Itami T, Sano T, Yamashita K.
 - J Vet Med Sci. 84:792-798. 2022. doi: 10.1292/jvms.21-0648.
 - 3) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia.
 - Hanazono K, Nakamoto M, Hori A, Miyoshi K, Nakade T, Itami T, Sano T, **Kato K**, Ito A, Tanaka K, Yamashita K, Endoh D.
 - J Vet Med Sci. 84:1556-1562. 2022. doi: 10.1292/jvms.22-0122.

RESEARCH PAPER

Effects of sevoflurane, propofol or alfaxalone on neuromuscular blockade produced by a single intravenous bolus of rocuronium in dogs

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Abstract

Objective To compare the effects of sevoflurane, propofol and alfaxalone on the neuromuscular blockade induced by a single intravenous bolus of rocuronium in dogs.

Study design A randomized, prospective, crossover experimental study.

Animals A total of eight adult Beagle dogs (four female, four male), weighing $8.9{-}15.3~{\rm kg}$ and aged $5{-}7~{\rm years}$.

Methods The dogs were anesthetized three times with $1.25\times$ minimum alveolar concentration of sevoflurane (SEVO treatment) and $1.25\times$ minimum infusion rate of propofol (PROP treatment) or alfaxalone (ALFX treatment) at intervals of ≥14 days. Neuromuscular function was monitored with train-of-four (TOF) stimulation of the peroneal nerve by acceleromyography. After recording the control TOF ratio (TOFRC), a single bolus dose of rocuronium (1 mg kg $^{-1}$) was administered intravenously. The times from rocuronium administration to achieving TOF count 0 (onset time), from achieving TOF count 0 to the reappearance of TOF count 4 (clinical blockade period), from 25% to 75% of TOFRC (recovery index) and from achieving TOF count 0 to TOF ratio/TOFRC >0.9 (total neuromuscular blockade duration) were recorded.

Results The onset time and recovery index did not differ among the treatments. The median clinical blockade period was longer in the SEVO treatment [27.3 (26.0–30.3) minutes] than in PROP [16.6 (15.4–18.0) minutes; p=0.002] and ALFX [22.4 (18.6–23.1) minutes; p=0.017] treatments; and longer in the ALFX treatment than in the PROP treatment (p=0.020). The mean total neuromuscular blockade duration was longer in the SEVO treatment

 $(43.7 \pm 9.9 \text{ minutes})$ than in PROP $(25.1 \pm 2.7 \text{ minutes}; p < 0.001)$ and ALFX $(32.5 \pm 8.4 \text{ minutes}; p = 0.036)$ treatments.

Conclusions and clinical relevance Compared with alfaxalone and propofol, sevoflurane prolonged rocuroniuminduced neuromuscular blockade by a significantly greater extent in dogs.

Keywords alfaxalone, dogs, neuromuscular blockade, propofol, rocuronium, sevoflurane.

Introduction

Rocuronium bromide, an aminosteroid, is a nondepolarizing neuromuscular blocking agent (NMBA). It has a faster onset as compared with that of vecuronium, but the duration of action is similar between the two (Marshall et al. 1994; Larijani et al. 1995; Kansanaho et al. 1997). Currently, rocuronium has widespread clinical application in veterinary practice and has been administered to dogs through intravenous (IV) boluses, incremental IV doses or constant rate infusion (CRI) to improve skeletal muscle relaxation during surgical procedures under general anesthesia (Dugdale et al. 2002; Alderson et al. 2007; Aucr et al. 2007; Briganti et al. 2015; Haga et al. 2019). However, administration of NMBAs may lead to a residual block, which is the presence of a neuromuscular blockade during the postoperative period (sones et al. 2015). Studies in humans have shown that sex, body weight, body temperature, concentration of volatile anesthetic agents and interval between the last NMBA administration and reversal agent administration are associated with a residual block (Vanlinthout et al. 1996; Srivastava & Hunter 2009; Khamtuikeua et al. 2017; Saager et al. 2019).

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The Journal of Veterinary Medical



Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits

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ARSTRACT. Recently, a mucosal atomization device (MAD) has been applied in veterinary medicine. In the present study, the maximum volume of nasal atomization without aspiration using MAD was examined in eight healthy female Japanese White (JW) rabbits. Each rabbit had their head and neck examined by computed tomography before and after nasal atomization with four different doses (0.15, 0.3, 0.45, and 0.6 ml per nostril) of diluted contrast medium (1:2 mixture of lohexol and saline). This was done under general anesthesia by an intramuscular administration of alfaxalone 2.5 mg/kg, medetomidine 40 µg/kg, and butorphanol 0.4 mg/kg, with a 7-day washout period between each treatment. The diluted contrast medium was distributed in the nasal cavity, external nares, and/or oral cavity in all rabbits receiving each treatment. The intranasal distribution volumes of the contrast medium were 287 (250-333) mm³ (median (interquartile range)) for 0.15 ml, 433 (243-555) mm⁸ for 0.3 ml, 552 (356-797) mm⁸ for 0.45 ml, and 529 (356-722) mm³ for 0.6 ml of treatment. The intranasal distribution volume for 0.15 ml treatment tended to be lower than that for 0.6 ml treatment (P=0.083). The contrast medium was deposited in the trachea in one rabbit (12.5%) and four rabbits (50%) receiving treatments of 0.45 and 0.6 ml per nostril, respectively. The maximum volume of nasal atomization without aspiration into the trachea was 0.3 ml per nostril for the JW rabbits.

KEYWORDS: intranasal administration, mucosal atomization device (MAD), nasal atomization volume, rabbit

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The Journal of Veterinary Medical Science



FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC_s/Ao) and the ratio of long to short diameter of the CVC (CVC_L/CVC_L) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intraabdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC_s/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low M8P group had significantly higher CVCs/Ao of the thorax than the normal M8P group. The group with intra-abdominal mass had significantly lower CVCs/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/ CVC_5 of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₅/Ao of the thorax, $\text{CVC}_{\text{L}}/\text{CVC}_{\text{S}}$ of the thorax, $\text{CVC}_{\text{L}}/\text{Ao}$ of the abdomen, and $\text{CVC}_{\text{L}}/\text{CVC}_{\text{S}}$ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Mid-to-caudal partial hemipelvectomy with limb preservation for ischial tumor in a dog.

Endo Y, <u>Sakai T</u>, Fukui S, Hori A, Ryosuke E, Matsunaga S, Kadosawa T. *J Vet Med Sci.* Feb; 84(2): 218–222. 2022. doi: 10.1292/jvms.21-0414

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1011

Surger

Mid-to-caudal partial hemipelvectomy with limb preservation for ischial tumor in a dog

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ABSTRACT. A 10-year-old spayed female Golden Retriever was referred for hindlimb lameness. A firm mass was palpated over the right caudal pelvis. Computed tomography revealed an osteolytic bone region and an associated periosteal reaction in the ischium, including the acetabulum. The histological diagnosis was sarcoma of unknown origin. A mid-to-caudal partial hemipelvectomy was performed to remove the mass. Femoral head and neck osteotomy was performed to allow hindlimb preservation. Following surgery, the dog regained satisfactory hindlimb use over time and was alive for 821 days with no recurrence or metastatic disease. This report indicates that mid-to-caudal partial hemipelvectomy with femoral head and neck osteotomy is technically feasible and allows for tumor control with preservation of the hindlimb and its function.

KEY WORDS: dog, femoral head and neck osteotomy, limb preservation, mid-to-caudal hemipelvectomy, pelvic tumor

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- 1) Relationship between *Escherichia coli* virulence factors, notably *kpsMTII*, and symptoms of clinical metritis and endometritis in dairy cows

Yamamura F, <u>Sugiura T</u>, Mumby M, Shiokura S, Murata R, Nakamura T, Fujiki J, and Iwano H

J Vet Med Sci. 2022 Mar; 84(3): 420-428. doi: 10.1292/jvms.21-0586



FULL PAPER

Theriogenology

Relationship between *Escherichia coli* virulence factors, notably *kpsMTII*, and symptoms of clinical metritis and endometritis in dairy cows

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ABSTRACT. Although Escherichia coli is a commensal bacterium of the bovine vaginal microbiota, it is an important pathogenic bacterium that causes diseases of the reproductive tract and subfertility. Recent studies have focused on virulence factors (VFs) of intrauterine E. coli; however, actual endometrial VFs have not been clearly identified. The purpose of this study was to identify the VFs of E. coli associated with clinical metritis and endometritis. Thirty-two strains of E. coli and four mixed Trueperella pyogenes (TP) strains were detected in the uterus of 19 Holstein dairy cows with obvious clinical signs (between 8 and 66 days postpartum). The presence of six E. coli VFs (fimH, fyuA, kpsMTII, hra1, csgA, and astA) was examined by PCR, and clinical signs and reproductive performance (mixed TP, the percentage of polymorphonuclear neutrophils [PMN%], days to uterine involution, etc.) were evaluated. Four VFs (fimH, hra1, csgA, and astA) were detected in all E. coli strains, whereas fyuA and kpsMTII were detected in 94% and 50% of strains, respectively. Cows with E. coli strains harboring kpsMTII exhibited significantly severe clinical scores (vaginal discharge score, PMN%, uterine involution), suggesting that kpsMTII is a key VF for progression of clinical metritis and endometritis. In the present study, we clearly identified six VFs associated with clinical metritis and endometritis. In addition, E. coli strains with kpsMTII probably play a crucial role in the progression of clinical metritis and endometritis.

KEY WORDS: Escherichia coli, kpsMTII, postpartum uterine disease, uterine restoration time, virulence factor

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- II. その他<Others>
 - 1) Exploration of serum biomarkers in dogs with malignant melanoma receiving anti-PD-L1 therapy and potential of COX-2 inhibition for combination therapy.

 Maekawa N, Konnai S, Asano Y, Sajiki Y, **Deguchi T**, Okagawa T, Watari K,
 Takeuchi H, Takagi S, Hosoya K, Kim S, Ohta H, Kato Y, Suzuki Y, Murata S,
 Ohashi K.

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scientific reports



OPEN

Exploration of serum biomarkers in dogs with malignant melanoma receiving anti-PD-L1 therapy and potential of COX-2 inhibition for combination therapy

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Immune checkpoint inhibitors (ICIs) such as anti-PO-L1 antibodies are widely used to treat human cancers, and growing evidence suggests that ICIs are promising treatments for canine malignancies. However, only some canine oral malignant melanoma (OMM) cases respond to ICIs. To explore biomarkers predictive of survival in dogs with pulmonary metastatic OMM receiving the anti-PD-L3. antibody c4G12 (n = 27), serum concentrations of prostaglandin E2 (PGE₂), cytokines, chemokines, and growth factors were measured prior to treatment initiation. Among 12 factors tested, PGE₂, interleukin (II.)-12p40, IL-8, monocyte chemotactic protein-1 (MCP-1), and stem cell factor (SCF) were higher in OMM dogs compared to healthy dogs (n = 8). Further, lower baseline serum PGE, MCP-1, and vascular endothelial growth factor (VEGF)-A concentrations as well as higher IL-2, IL-12, and SCF concentrations predicted prolonged overall survival. These observations suggest that PGE2 confers resistance against anti-PD-L1 therapy through immunosuppression and thus is a candidate target for combination therapy, indeed, PGE, suppressed IL-2 and interferon (IFN)-y production by stimulated canine peripheral blood mononuclear cells (PBMCs), while inhibition of PGE, biosynthesis using the COX-2 inhibitor meloxicam in combination with c4G12 enhanced Th1 cytokine production by PBMCs. Thus, serum PGE, may be predictive of c4G12 treatment response, and concomitant use of COX-2 inhibitors may enhance ICI antitumor efficacy.

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- 1) 12-HETE promotes late-phase reactions in a murine model of allergic rhinitis.
 Nakamura T*, Tachibana Y*, Murata T.
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1) The effect of exposure on cattle thyroid after the Fukushima Daiichi nuclear power plant accident.

Horikami D, Sayama N, Sasaki J, Kusuno H, Matsuzaki H, Hayashi A, <u>Nakamura T</u>, Satoh H, Natsuhori M, Okada K, Ito N, Sato T, Murata T.

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scientific reports



OPEN The effect of exposure on cattle thyroid after the Fukushima Daiichi nuclear power plant accident

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Nuclear plant accidents can be a risk for thyroid cancer due to iodine radioisotopes. Near the Fukushima Dalichi nuclear power plant, cattle were exposed to radiation after the accident occurred in May 2011. Here we estimated the total radiation exposure to cattle thyroid and its effects on thyroid function. Until October 2016, the estimated external exposure dose in Farm A was 1416 mGy, while internal exposure dose of ¹³¹l, ¹³⁶Cs, and ¹³⁷Cs were 85, 8.8, and 9.7 mGy in Farm A and 34, 0.2, and 0.3 mGy in Farm B, respectively. The exposed cattle had thyroid with relatively lower weight and lower level of stable iodine, which did not exhibit any pathological findings. Compared with the control, the plasma level of thyroid-stimulating hormone (TSH) was higher in Farm A cattle born before the accident, while the plasma thyroxine (T4) was higher in Farm A cattle born after the accident, suggesting that exposed cattle showed slight hyperactivation of the thyroid gland. In addition, Farm A cattle have higher level of cortisol, one of the anterior pituitary gland-derived hormones. However, we did not observe a causal relationship between the radiation exposure and cattle thyroid.

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Urinary lipid profile of patients with coronavirus diseases 2019

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The coronavirus diseases 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is ongoing. Over 490 million people have been infected with this virus worldwide. Although many patients present with lower respiratory symptoms, some may progress to acute respiratory distress syndrome and even multi-organ damage. Therefore, there is an urgent need to establish treatment and management methods for this infectious disease. Here, we comprehensively analyzed urinary lipid mediators and their metabolites to identify non-invasive biomarkers that reflect the disease status of COVID-19 patients. We diagnosed 16 patients by polymerase chain reaction (PCR) analysis, who presented with mild-tomoderate symptoms, including fever and cough, between May and October 2020 in Japan, and collected their urine samples. Using mass spectrometry, we analyzed the lipid metabolites in these urine samples. In all the urine samples from the patients, 21 types of fatty acids and their metabolites were consistently detected in the samples among the 214 metabolites which were analyzed. Interestingly, urinary levels of fatty acids, docosahexaenoic acid was increased by approximately 3-fold in patients with COVID-19 compared to those in healthy subjects. Metabolites of major proinflammatory lipid mediators, PGE2, TXA2, and PGF2a, were also detected at significantly higher levels in the urine of patients with COVID-19. These observations suggest that urinary lipids can reflect the inflammatory status of patients with COVID-19, which can be a useful index to manage this disease.

B F Y NECTOR FO

COVID-19, lipidomics, proinflammatory lipid mediators, metabolites, urine analysis

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HOTE

Physiology

Urinary lipid production profile in canine patients with splenic mass

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ABSTRACT. Polyunsaturated fatty acids (PUFAs), including arachidonic acid (AA), docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA), are metabolized to various lipid mediators. The profile of these lipid metabolites excreted into the urine reflects inflammatory state of the body and disease conditions. In this study, we quantified 156 types of lipids in urine samples of dogs with splenic mass, using liquid chromatography-tandem mass spectrometry. We found that metabolites of prostaglandin (PG) E_2 , $F_{2\alpha}$, and D_2 , 8-iso-PGF $_{3\alpha}$, lyso-platelet activating factor, and 14,15-leukotrien C_4 significantly increased in urine samples of dogs with splenic mass compared to that of healthy dogs. These observations may reflect general inflammatory responses and will help better understanding of the canine splenic mass.

KEYWORDS: dog, lipid metabolite, splenic mass, urine

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Physiology

Comprehensive profiling of lipid metabolites in urine of canine patients with liver mass

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gaining insights into the disease. These findings may also have an application as a screening test or

ABSTRACT. Fatty acids are an essential component of mammalian bodies. They go through different metabolic pathways depending on physiological states and inflammatory stimuli. In this study, we conducted a liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based comprehensive analysis of lipid metabolites in urine of canine patients with liver mass. There were significant differences in quantity of some lipid metabolites that may be closely associated with the disease and/or general inflammatory responses, including increased metabolites of prostaglandin E₂ and/or PGF₂₀. We demonstrated that our approach of profiling lipid metabolites in the urine is useful in

a diagnosis tool for canine liver mass.
KEYWORDS: dog, liver mass, lipid metabolite, urine

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Physiology

The urinary lipid profile in cats with idiopathic cystitis

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J. Vet. Med. Sci. 84(5): 689–693, 2022 doi: 10.1292/jvms.22-0049

Received: 28 January 2022 Accepted: 24 March 2022 Advanced Epub: 5 April 2022 ABSTRUCT. Although feline idiopathic cystitis (FIC) distresses of many cats, its pathogenesis is unknown and the diagnosis is challenging. Polyunsaturated fatty acids (PUFAs) are metabolized into various lipid mediators. Lipid mediators such as prostaglandins (PGs) modulate inflammation and many of them are excreted into the urine. Thus, the investigation of the urinary lipid profile may reveal pathogenesis and help diagnosis of FIC. We collected urine samples from five FIC cats by spontaneous urination and analyzed 158 types of lipid mediators in urines using liquid chromatography-mass spectrometry. The urinary levels of PUFAs were higher in FIC compared to those of the healthy group. The excretions of a major inflammatory mediator, PGD2, were less in FIC. Other well-known inflammatory mediators such as PGE2, PGI2, and their metabolites did not show a difference. In contrast, the levels of PGF2 α and its 2 metabolites and PGF3 α were higher in FIC. These results may provide new insights into the future management of cat FIC.

KEYWORDS: feline idiopathic cystitis, lipid mediator, prostaglandin, urine

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Physiology

The profile of urinary lipid metabolites in healthy dogs

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J. Vet. Med. Sci. 84(5): 644–647, 2022 doi: 10.1292/jvms.22-0020

Received: 18 January 2022 Accepted: 5 March 2022 Advanced Epub: 23 March 2022 ABSTRACT. Polyunsaturated fatty acids, including arachidonic acid (AA), docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA), are converted to hundreds of lipid mediators by cyclooxygenases (COX), lipoxygenases (LOX), and cytochrome P450 (CYP), or through non-enzymatic processes, and they reflect inflammatory states of the body. We comprehensively analyzed lipid metabolites in dog urine using a liquid chromatograph-mass spectrometry (LC-MS/MS) to describe their metabolic characteristics. We detected 31 AA-derived metabolites, four EPA-derived metabolites, and a DHA-derived metabolite in all urine samples. Among AA-derived metabolites, 15, 5, 3, and 8 were generated by COX, LOX, CYP, and non-enzymatic oxidation respectively. This study will be the first step to use profiles of urinary lipid metabolites for better understanding and diagnosis of canine diseases.

KEYWORDS: dog, lipid metabolite, urine

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RESEARCH ARTICLE



15-hydroxy eicosadienoic acid is an exacerbating factor for nasal congestion in mice

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Abstract

Allergic rhinitis (AR) is one of the most common allergic inflammatory diseases worldwide. In AR, increased blood flow and vascular permeability in nasal mucosa cause rhinorrhea and nasal congestion. We investigated the role of an 11Z,14Z-eicosadienoic acid-derived metabolite, 15-hydroxy-11Z,13Z-eicosadieno ic acid (15-HEDE), in functional changes in vasculature and nasal congestion in AR. Repeated intranasal administration of Ovalbumin (OVA) caused AR symptoms, such as sneezing and nasal congestion, in mice. OVA administration increased the level of 15-HEDE in nasal lavage fluid, which reached approximately 0.6 ng/ml after ten OVA treatments. Upon measuring vascular contraction, treatment with 0.1-3 μM 15-HEDE did not cause contraction in mouse aortae, while it dilated aortae that were pre-contracted by thromboxane receptor stimulation. Pretreatment with the voltage-gated $K^+(K_V)$ channel inhibitor 4-aminopyridine significantly inhibited the 15-HEDE-induced vascular relaxation. Intravital imaging showed that administration of 1 μ g 15-HEDE dilated blood vessels, and Mile's assay demonstrated that this administration also caused dye leakage, indicating vascular hyperpermeability in mouse ears. Computed tomography scanning and morphological study revealed that administration of 3 μg 15-HEDE narrowed nasal passages and thickened nasal mucosa in mice. Finally, we confirmed that treating mice with 3 µg 15-HEDE caused rhinitis symptoms, such as abdominal breathing, and reduced respiratory frequency, suggesting nasal congestion. 15-HEDE caused vasodilation by activating K_V channels and increased vascular permeability, which may lead to nasal congestion. Furthermore, 15-HEDE might be a new lipid mediator that exacerbates nasal congestion in AR.

KEYWORDS

animal models, fatty acid, inflammation, oxidized lipids, vascular biology

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実験動物学 (Laboratory animal sciences)

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助教 藤本 政毅

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Preclinical studies for improving radiosensitivity of non-small cell lung cancer cell lines by combining glutaminase inhibition and senolysis

Fujimoto M, Higashiyama R, Yasui H, Yamashita K, Inanami O.

Translational Oncology, 21: 101431. 2022. doi: /10.1016/j.tranon.2022.101431

- 2) Ubiquitin-Specific Protease 2 in the Ventromedial Hypothalamus Modifies Blood Glucose Levels by Controlling Sympathetic Nervous Activation Hashimoto M, <u>Fujimoto M</u>, Konno K, Lee M, Yamada Y, Yamashita K, Toda C, Tomura M, Watanabe M, Inanami O, Kitamura H.
 - J. Neurosci. 42 (23):4607-4618. 2022. doi: 10.1523/jneurosci.2504-21.2022
- 3) Application of the colorimetric loop-mediated isothermal amplification (LAMP) technique for genotyping Cre-driver mice

Fujimoto M, Kitamura H.

JVMS. .84 (4), 507-510.2022, doi: 10.1292/jvms.21-0658

Ⅱ. その他<Others>

1) Eribulin improves tumor oxygenation demonstrated by 18F-DiFA hypoxia imaging, leading to radio-sensitization in human cancer xenograft models
Bo T, Yasui H, Shiga T, Shibata Y, Fujimoto M, Suzuki M, Higashikawa K, Miyamoto N, Inanami O, Kuge Y.

Eur. J. Nucl. Med. Mol. Imaging. 49: 821-833. 2022. doi: 10.1007/s00259-021-05544-4



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Original Research

Preclinical studies for improving radiosensitivity of non-small cell lung cancer cell lines by combining glutaminase inhibition and senolysis

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ARTICLE INFO

Keywords: Radiation Glutaminolysis Senescence Senolytic drug Apoptosis

ABSTRACT

Glutamine metabolism, known as glutaminolysis, is abnormally activated in many cancer cells with KRAS or BRAF mutations or active c-MYC. Glutaminolysis plays an important role in the proliferation of cancer cells with oncogenic mutations. In this study, we characterized radiation-induced cell death, which was enhanced by glutaminolysis inhibition in non-small cell lung cancer A549 and H460 cell lines with KRAS mutation. A clonogenic survival assay revealed that treatment with a glutaminase inhibitor, CB839, enhanced radiosensitivity. X-irradiation increased glutamate production, mitochondrial oxygen consumption, and ATP production, whereas CB839 treatment suppressed these effects. The data suggest that the enhancement of glutaminolysis-dependent energy metabolism for ATP production is important for survival after X-irradiation. Evaluation of the cell death phenotype revealed that glutaminolysis inhibitory treatment with CB839 or a low-glutamine medium significantly promoted the proliferation of β -galactosidase-positive and IL-6/IL-8 secretory cells among X-irradiato tumor cells, corresponding to an increase in the senescent cell population. Furthermore, treatment with ABT263, a Bcl-2 family inhibitor, transformed senescent cells into apoptotic cells. The findings suggest that combination treatment with a glutaminolysis inhibitor and a senolytic drug is useful for efficient radiotherapy.

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最終責任者 Osamu Inanami (Corresponding Author)

Cellular/Molecular

Ubiquitin-Specific Protease 2 in the Ventromedial Hypothalamus Modifies Blood Glucose Levels by Controlling Sympathetic Nervous Activation

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Ubiquitin-specific protease 2 (USP2) participates in glucose metabolism in peripheral tissues such as the liver and skeletal muscles. However, the glucoregulatory role of USP2 in the CNS is not well known. In this study, we focus on USP2 in the ventromedial hypothalamus (VMH), which has dominant control over systemic glucose homeostasis. ISH, using a *Usp2*-specific probe, showed that *Usp2* mRNA is present in VMH neurons, as well as other glucoregulatory nuclei, in the hypothalamus of male mice. Administration of a USP2-selective inhibitor ML364 (20 ng/head), into the VMH elicited a rapid increase in the circulating glucose level in male mice, suggesting USP2 has a suppressive role on glucose mobilization. ML364 treatment also increased serum norepinephrine concentration, whereas it negligibly affected serum levels of insulin and corticosterone. ML364 perturbated mitochondrial oxidative phosphorylation in neural SH-SY5Y cells and subsequently promoted the phosphorylation of AMP-activated protein kinase (AMPK). Consistent with these findings, hypothalamic ML364 treatment stimulated AMPKα phosphorylation in the VMH. Inhibition of hypothalamic AMPK prevented ML364 from increasing serum norepinephrine and blood glucose. Removal of ROS restored the ML364-evoked mitochondrial dysfunction in SH-SY5Y cells and impeded the ML364-induced hypothalamic AMPKα phosphorylation as well as prevented the elevation of serum norepinephrine and blood glucose levels in male mice. These results indicate hypothalamic USP2 attenuates perturbations in blood glucose levels by modifying the ROS-AMPK-sympathetic nerve axis.

Key words: hypothalamus; mitochondria; reactive oxygen species; ubiquitin-specific protease 2; ventromedial hypothalamus

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Laboratory Animal Science

Application of the colorimetric loopmediated isothermal amplification (LAMP) technique for genotyping *Cre*-driver mice

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ABSTRACT. The Cre-loxP system is widely used to investigate the cell-type specific roles of genes of interest. Cre-driver mice are required for cell-type specific knockout during the Cre-loxP reaction. To maintain Cre-driver mouse strains, Polymerase chain reaction (PCR)-oriented genotyping targeting the Cre gene cassette is usually conducted. In this study, we instead applied a colorimetric loop-mediated isothermal amplification (LAMP) method for Cre-genotyping. Among four sets of primers designed by the in silico program, one set effectively amplified the Cre cassette of three Cre-driver strains, but not of C57BL/6 mice. This LAMP-oriented method reduces assay time by less than half compared to the PCR-based method, and can be carried out using a conventional isothermal incubator. Applying this LAMP method may accelerate genotyping of Cre-driver mice.

KEYWORDS: conditional knockout, Cre, genotyping, loop-mediated isothermal amplification

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ORIGINAL ARTICLE



Eribulin improves tumor oxygenation demonstrated by ¹⁸F-DiFA hypoxia imaging, leading to radio-sensitization in human cancer xenograft models

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Abstract

Purpose Eribulin, an inhibitor of microtubule dynamics, is known to show antitumor effects through its remodeling activity in the tumor vasculature. However, the extent to which the improvement of tumor hypoxia by eribulin affects radio-sensitivity remains unclear. We utilized 1-(2,2-dihydroxymethyl-3-18F-fluoropropyl)-2-nitroimidazole (18F-DiFA), a new PET probe for hypoxia, to investigate the effects of eribulin on tumor hypoxia and evaluate the radio-sensitivity during eribulin treatment. Methods Mice bearing human breast cancer MDA-MB-231 cells or human lung cancer NCI-H1975 cells were administered a single dose of eribulin. After administration, mice were injected with 18F-DiFA and pimonidazole, and tumor hypoxia regions were analyzed. For the group that received combined treatment with radiation, 18F-DiFA PET/CT imaging was performed before tumors were locally X-irradiated. Tumor size was measured every other day after irradiation.

Results Eribulin significantly reduced ¹⁸F-DiFA accumulation levels in a dose-dependent manner. Furthermore, the reduction in ¹⁸F-DiFA accumulation levels by eribulin was most significant 7 days after treatment. These results were also supported by reduction of the pimonidazole-positive hypoxic region. The combined treatment showed significant retardation of tumor growth in comparison with the control, radiation-alone, and drug-alone groups. Importantly, tumor growth after irradiation was inversely correlated with ¹⁸F-DiFA accumulation.

Conclusion These results demonstrated that ¹⁸F-DiFA PET/CT clearly detected eribulin-induced tumor oxygenation and that eribulin efficiently enhanced the antitumor activity of radiation by improving tumor oxygenation.

Keywords Eribulin · 18F-DiFA · Hypoxia · Radiation · PET/CT imaging

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Expression of indian hedgehog signaling in murine oviductal infundibulum and its relationship with epithelial homeostasis.

Hosotani M, Ichii O, Namba T, Masum MA, Nakamura T, Hasegawa Y, Watanabe T, Kon Y.

Cell Tissue Res. 2022. doi: 10.1007/s00441-022-03722-w

2) The histopathological features of the surgical endometriosis model using systemic autoimmune disease-prone mice.

Hosotani M, Akita M, Ueda H, Watanabe T.

J Vet Med Sci. 2022. doi: 10.1292/jvms.22-0442

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Comp Biochem Physiol A Mol Integr Physiol. 273:111296. 2022. doi: 10.1016/j.cbpa.2022.111296

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Makida S, Kametani K, <u>Hosotani M</u>, Takahashi N, Iwasaki T, Hasegawa Y, Takaya T, Ueda H, Watanabe T.

J Vet Med Sci. 84: 809–816. 2022. doi: 10.1292/jvms.22-0080

REGULAR ARTICLE



Expression of Indian hedgehog signaling in murine oviductal infundibulum and its relationship with epithelial homeostasis

Marina Hosotani¹⊕ · Osamu Ichii².³ · Takashi Namba² · Md. Abdul Masum² · Teppel Nakamura².⁴ · Yasuhiro Hasegawa⁵ · Takafumi Watanabe¹ · Yasuhiro Kon²

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Abstract

Homeostasis of the oviductal infundibulum epithelium is continuously regulated by signaling pathways under physiological and pathological conditions. Herein, we investigated the expression of hedgehog (Hh) signaling-related components in the murine oviductal infundibulum, which is known to maintain homeostasis in the adult epithelium. Additionally, using autoimmune disease-prone MRL/Mpl-Fas^{fis/lpr} (MRL/lpr) mice showing abnormal morphofunction of the ciliated epithelium of the infundibulum related to the oviductal inflammation, we examined the relationship between Hh signaling and pathology of the infundibulum. The expression and localization of Pax8, a marker for progenitor cells in the oviductal epithelium, and Foxjl, a marker for ciliogenesis, were examined in the infundibulum. The results showed that Pax8 was downregulated and Foxjl was upregulated with aging, suggesting that homeostasis of the infundibulum epithelium of MRL/lpr mice was disturbed at 6 months of age. In all mice, the motile cilia of ciliated epithelial cells in the infundibulum harbored Hh signaling pathway-related molecules: patched (Ptch), smoothened (Smo), and epithelial cells harbor Gli. In contrast, Ptch, Smo, and Gli2 were significantly downregulated in the infundibulum of MRL/lpr mice at 6 months of age. The expression levels of Pax8 and FaxJ1 were significantly positively correlated with those of Ptch1, Smo, and Gli2. Hh signaling is thought to be involved in homeostasis of the ciliated epithelium in the infundibulum. In MRL/lpr mice, which show exacerbated severe systemic autoimmune abnormalities, molecular alterations in Hh signaling-related components are considered to interact with local inflammation in the infundibulum, leading to disturbances in epithelial homeostasis and reproductive function.

Keywords Autoimmune abnormality · Ciliated epithelium · Hedgehog signaling pathway · Homeostasis · Oviduct

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Introduction

Mammalian oviducts are divided into three parts, the infundibulum, ampulla, and isthmus, in order from the distal to proximal parts. The different composition ratios of ciliated epithelial cells and secretory cells in the epithelium of each part reflect the unique reproductive function in each section (Li et al. 2017; Koyama et al. 2019). Particularly, the infundibulum epithelium is composed mostly of ciliated epithelial cells, so that ciliary beating effectively moves occytes produced in the ovaries into the oviductal lumen; this process is known as oocyte pick-up. Oocyte pick-up and transportation are disturbed by abnormal ciliary morphofunction in the infundibulum caused by pathological conditions such as smoking (Talbot and Riveles 2005), hormonal dysregulation (Raidt et al. 2015), and inflammation (Hosotani et al. 2020). Physiologically, the proportion of ciliated epithelial cells and secretory cells in the infundibulum epithelium changes under hormonal dynamics through the

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最終責任者 Marina Hosotani (First and Corresponding Author)

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The histopathological features of the surgical endometriosis model using systemic autoimmune disease-prone mice

Marina HOSOTANI, Machiko AKITA, Hiromi UEDA, Takafumi WATANABE

Author information

Keywords; autoimmune disease, endometriosis, immune cell, surgical model, uterus

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Abstract

Endometriosis is a common gynecological disease that affects women of reproductive age in which the uterine endometrium grows outside the uterus. Origin of the ectopic endometrium is thought to be the retrograde endometrium through the oviducts. However, factors that determine the adherence and proliferation of the ectopic endometrium have not been revealed, importantly, systemic autoimmune diseases are considered a key factor in the endometriosis onset. Herein, we established a surgical endometriosis rodent model using autoimmune disease-prone MRL/MpJ-Faslor/lpr (MRL/lpr) and MRL/+ mice to provide basic evidence of the relationship between autoimmune disease and endometriosis. Endometriosis lesions were successfully induced in two regions after transplanting uterine tissues from donor mice into the peritoneal cavity of recipient mice: the peritoneum or adipose tissue around the transplantation point (proximal lesions) and the gastrosplenic ligament or intestinal mesentery far from the transplantation site (distal lesions). Distal lesions were observed only in MRL/lpr mice, whereas endometriosis lesions showed no genotype- or regionrelated differences in the histology and distribution of sex hormone receptors and Ticells. In contrast, transplanted uterine tissues in donor MRL/lpr mice exhibited a large infiltration of T cells in the lamina propria. Splenomegaly was more common in recipient than that in donor MRL/lpr mice. These results suggest that the infiltration of endogenous T cells in the endometrium alters the growth features of ectopic endometrium, possibly affecting the severity of endometriosis in patients with systemic autoimmune diseases.

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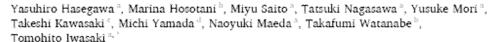
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Mitochondrial characteristics of chicken breast muscle affected by wooden breast



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ABSTRACT

The growth rate of broiler chickens has increased by 400% over the past 50 years, and breast yields continue to increase. This has led to an increase in thoracic muscle abnormalities in broilers, with wooden breast becoming a major issue worldwide. The etiology and the mechanism underlying the etiology of wooden breasts have not yet been elucidated; however, it occurs due to oxidative stress. Reactive oxygen species, which cause oxidative stress, are mainly produced in mitochondria. Thus, in this study, we investigated the relationship between the severity of wooden breast in broilers and the characteristics of mitochondria as the source of reactive oxygen species. Sampling of the pectoralis major muscle at the ventral cranial position was conducted in 50-day-old broilers. The severity of wooden breast was classified into three groups based on the muscle fiber roundness and wing-wing contact test, with highest severity in severe wooden breast and lowest severity in normal breast. Nicotinamide adenine dinucleotide tetrazolium reductase staining revealed an increase in darkly stained muscle fibers, indicating high severity of wooden breast. The mitochondria were swollen in severe wooden breast cases, with highest swelling in severe wooden breast and lowest swelling in normal breast. The expression levels of the misochondrial antioxidant enzyme genes superoxide dismutase 1 and superoxide dismutase 2 were significantly lower in wooden breast-severe tissue than in normal tissue. These results suggest that when the levels of reactive oxygen species in muscle fibers, which should be constant, are increased, mitochondrial homeostasis is not maintained and the damage levels increase in various membranes of the cell, leading to the disruption of normal physiological functions.

1. Introduction

Chicken is the most commonly consumed meat in the world. To obtain higher meat yields from improved breeding, chickens with large breast muscles have been selected as broilers. This has led to a 50% decrease in their feed conversion ratio over the past 50 years, with a 400% increase in their growth rate; thus, chickens with substantial amounts of breast meat are currently produced (Tuidhof et al., 2014). However, with high productivity, abnormally hard breast meat emerging from a condition known as wooden breast are observed; this is a worldwide problem as the breast meat loses its commercial value (Xing et al., 2020). Breast muscles affected by wooden breast are pale in color,

markedly hardened, diffusely or focally clear, and slightly turbid; moreover, moderate levels of viscous materials and/or petechiae can be found on the fillet surface (Clark and Vellessam, 2016; Silvo et al., 2014). Previous studies have identified the specific histopathological characteristics of wooden breast muscles, which include muscle fiber roundness, abundant adipose tissue infiltration, and increased amount of connective tissue due to the thickening of collagen fiber bundles (Hasegawa et al., 2021; Silvo et al., 2014).

Mitochondria are essential organelles, which account for 90% of cellular oxygen consumption and contribute the most to ATP synthesis (Herd and Arthur, 2009). The mitochondrial electron transport chain is involved in tissue oxygen consumption and generates reactive oxygen

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The Journal of Veterinary Medical Science



FULL PAPER

Morphological analysis of cell distribution and network structure via gap junctions in swine corneal stroma

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ABSTRACT. Because of corneal transplantation limitations, there is a need for cornea-specific regenerative medicine. The development of such regenerative medicine has been delayed because of the complex and unique structure of the corneal stroma. Few studies have explored the corneal stroma cell distribution and cell types in vivo. This study investigated regional differences in morphological characteristics and distributions of corneal keratocytes and immunocompetent cells in the corneal stroma to clarify their functions and structural characteristics. The porcine eyeballs were subjected to light microscopy, transmission electron microscopy, scanning electron microscopy, and immunofluorescence staining analyses. Corneal cells were primarily located in the limbus, rather than the center of the comea; the long keratocyte diameter was largest on the epithelial side of the corneal limbus, while the short diameter was largest on the endothelial side of the central comea. Moreover, there were significantly more comeal cells on the epithelial side than on the endothelial side in both the central and limbus areas. Gap junctions between cells in the corneal stroma were present on the surfaces of cytoplasmic processes. Many cytoplasmic processes were scattered throughout the corneal stroma; they were connected both vertically and horizontally, forming an intercellular network. Additionally, immunocompetent cells on the epithelial side suggested to participate in this network via gap junctions. The morphology of keratocytes and immunocompetent cells on the epithelial side suggests that they play important roles in comeal homeostasis.

KEYMOROS: corneal keratocytes, corneal stroma, electron microscopy, gap junction, swine

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The comea is located in the anterior 20% of the eye; this structure is non-vascular and is nourished by aqueous humor [2]. Additionally, the epithelial layer is a unique tissue that does not undergo keratinization or pigmentation; it remains transparent. The comea is divided into five layers: anterior corneal epithelium (corneal epithelium), anterior border plate (Bowman's membrane), corneal stroma, posterior border plate (Descemet's membrane), and posterior corneal epithelium (corneal endothelium). The corneal stroma consists of collagen fibers and corneal keratocytes [2]. The cornea is mostly collagen (i.e., 70% of its dry weight) [22]. Collagen fibrils in the corneal stroma are regularly arranged and form a thin laminar structure of approximately 1 µm thickness; fibrils travel in the same direction in an orderly manner [36]. They cross each other at a specific angle and are arranged parallel to the corneal surface, forming a comeal stromal layer of approximately 300 layers [36]. Collagen fibril diameter ranges from 20 to 30 nm, this uniform thickness and regular arrangement are essential for corneal transparency [36]. In addition to keratocytes, myeloid-derived migratory cells (e.g., lymphocytes, macrophages, and some granulocytes) are reportedly present in the corneal stroma [2, 25, 40]. The presence of antigen-presenting cells, such as Langerhans cells and dendritic cells, has recently been reported in the corneal epithelium, as well as the corneal stroma; it is presumably involved in rejection during transplantation [10, 11, 26, 40].

The overall corneal thickness differs between the central and limbal areas; the limbal area is thicker than the central area in humans, dogs, and cattle [24]. The overall thickness of the cornea is determined by collagen fibrils and proteoglycans [1, 9, 30, 33]. These

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<Research Note>

Immune Response in Chickens Vaccinated with Freeze-Thawed or Warmed Water-in-Oil Vaccine

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This study investigated whether freezing or warming water-in-oil (W/O) vaccines affected the immune responses of chickens. One of the conditions affecting the efficacy of commercially available animal vaccines is the storage temperature range. Previous studies have shown that the properties of some inactivated vaccines change owing to freezing, leading to reduced immune responsiveness after inoculation. In this study, we first determined the freezing temperatures of a commercial W/O vaccine using freezers maintained at -10, -13, -15, and -20°C. The results showed that the W/O vaccine froze from -10 to -12°C. Next, we evaluated the effect on antibody level transitions (sample-to-positive ratio) in 46-day-old broiler chickens vaccinated with the W/O vaccine that was maintained at -20°C, 5°C, and -10°C, in that order. In addition, the effect on antibody value transitions was evaluated in 45-day-old broiler chickens vaccinated with the W/O vaccines that were frozen and thawed between -20°C and 5°C repeatedly or warmed to 42°C. In these experiments, no remarkable effect of the freeze-thawing or warming treatments on antibody value transitions was observed. These results suggested that the efficacy of the W/O vaccine was not significantly affected when placed in a frozen environment or left in a room temperature environment of 42°C or lower for approximately 5 d. These data indicate the possibility of expanding the temperature range for handling W/O vaccines.

Key words: adjuvant, cold chain, freeze-thaw, handling temperature, storage temperature, water-in-oil vaccine

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Introduction

The storage temperature range is specified for commercially available animal vaccines to guarantee their efficacy. However, in Japan, it remains unclear whether these temperature ranges are strictly defined as handling conditions or as guidelines. Additionally, if freezing affects the quality of a vaccine, it must be avoided during handling and storage. In vaccine logistics, it is presumed that most of these precautions are observed, however, it is often impossible to handle vaccines within the stated temperature range. Previous studies

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The Journal of Foultry Science is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-Share-Alike 4.0 International License. To view the details of this license, please visit (https:// creativecommons.org/licenses/by-nc-as/4.0/). have shown that it is difficult to maintain a specified storage temperature range during vaccine transport (Matthias et al., 2007; Kartoglu and Milstien, 2014; Das et al., 2019; Falcón et al., 2020). This is not only a problem in countries with underdeveloped cold chains, but also in countries and regions with developed cold chains (Kartoglu and Milstien, 2014; Falcôn et al., 2020). In particular, the risk of inadvertent exposure to freezing temperatures has been overlooked worldwide (Falcón et al., 2020). This issue poses a severe problem for both veterinarians directing the use of vaccines, as well as for vaccine users. Veterinarians should instruct users not to vaccinate animals with these vaccines because they cannot guarantee the quality of vaccines whose storage temperature may have been outside the specified range. Furthermore, in the unlikely event that a handling error compromises the vaccine quality, the user suffers a direct disadvantage.

Currently, water-in-oil (W/O)-type vaccines are widely used as inactivated vaccines in chickens. This type of vaccine induces a strong and long-term immune response with a small amount of antigen (Aucouturier et al., 2001). This study

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The Journal of Veterinary Medical Science



FULL PARTE Anatomy

Three-dimensional structural analysis of mitochondria composing each subtype of fast-twitch muscle fibers in chicken

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ASSTRACT. In a previous study, the three-dimensional structures of mitochondria in type I and type IIb muscle fibers of chicken were analyzed. The study reported differences in the shape of the mitochondria and the distribution of lipid droplets. In this study, we three-dimensionally analyzed mitochondria and lipid droplets of type II muscle fiber subtypes IIa, IIb, and IIc of chicken lateral Biotibial muscle in the same field of view using correlative light electron microscopy (CLEM) and array tomography methods. The reconstructed images showed that the mitochondria of type IIa muscle fiber were thick and aligned along the myofibrils, and many lipid droplets were embedded in the mitochondria. The mitochondria of type lib muscle fibers were intermittent, aligned along the myofibrils, and showed contact between adjacent horizontal mitochondria. No lipid droplets were observed in type ilb muscle fiber. In type ilc muscle fiber, we observed irregularly shaped mitochondria with small diameters aligned along the myofibrils. Lipid droplets not only were embedded in the mitochondria but also existed independently in some cases, The combination of array tomography and CLEM methods enabled three-dimensional electron microscopic observation of mitochondria in different subtypes of type II muscle fibers. The subtypes of type ii muscle fibers differed in mitochondrial occupancy and morphology and in lipid droplet distribution, and characteristics that had been demonstrated biochemically were also demonstrated ultrastructurally

KEYWORDS: array tomography, correlative light electron microscopy, electron microscopy, fast skeletal muscle, mitochondria

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In general, mammalian skeletal muscle fibers are classified into type I and type II, and subtypes are classified according to the difference in myosin heavy chain isoforms. Mammalian type II muscle fibers include type IIa, type IIb, and type IIx. Type Ha muscle fibers undergo aerobic metabolism, and type IIb muscle fibers undergo anaerobic metabolism. Type IIx has a fatigue tolerance intermediate between type IIa and type IIb muscle fibers [5, 20]. In the past, myosin ATPase histochemistry was used as a method for histological classification of skeletal muscle fiber subtypes, but the process is complicated [6]. In recent years, immunohistochemistry using primary antibodies against the myosin heavy chain has become common as a more accurate and simpler classification method [19]

The subtypes of chicken skeletal muscle fibers are classified as type II, type IIa, type IIb, type IIc, and tonic type, depending on the myosin heavy chain isoform. The function of type IIc muscle fibers is unknown [17]. In a previous study, three-dimensional (3D) electron microscopic analysis of the mitochondria of chicken type I muscle fibers of gastrocnemius muscle and type IIb muscle fibers of pectoralis major muscle was reported [9]. In type I muscle fibers, large mitochondria were present in dense succession and lipid droplets were incorporated into the mitochondria, whereas in type IIb muscle fibers, small mitochondria were

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 - 1) Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits.

Yixian Wei, <u>Ai Hori</u>, I-Ying Chen, Haruka Tamogi, Taku Hirokawa, Keiko Kato, Takaharu Itam, Tadashi Sano, Kazuto Yamashita.

J Vet Med Sci. 2022 Jun 10;84(6):792-798. doi: 10.1292/jvms.21-0648.

Ⅱ. その他<Others>

Kato, Daiji Endoh

1) Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia.

Kiwamu Hanazono, Mako Nakamoto, <u>Ai Hori</u>, Kenjiro Miyoshi, Tetsuya Nakade, Takaharu Itami, Tadashi Sano, Keiko Kato, Akifumi Ito, Kakeru Tanaka, Kazuto Yamashita, Daiji Endoh

J Vet Med Sci. 2022 Nov 18;84(12):1556-1562. doi: 10.1292/jvms.22-0122.

2) Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography. Kiwamu Hanazono, Takaharu Itami, Ikuto Hayasaka, Kenjiro Miyoshi, **Ai Hori,** Keiko

Animals (Basel). 2022 May 4;12(9):1175. doi: 10.3390/ani12091175.

 Mid-to-caudal partial hemipelvectomy with limb preservation for ischial tumor in a dog. Yoshifumi Endo, Toshikazu Sakai, Sho Fukui, <u>Ai Hori</u>, Ryosuke Echigo, Satoru Matsunaga, Tsuyoshi Kadosawa

J Vet Med Sci. 2022 Feb 10;84(2):218-222. doi: 10.1292/jvms.21-0414.

4) The impact of coronavirus disease 2019 (COVID-19) in Japanese companion animal clinics.

Fukumoto F, Kimura Y, Tsutsumi A, <u>Hori A</u>, Tanaka A, Ukita M, Makita K *J Vet Med Sci*. 2022 Aug 1;84(8):1041-1050. doi: 10.1292/jvms.22-0072.



FULL PAPER

Surgery

Maximum volume of nasal administration using a mucosal atomization device without aspiration in Japanese White rabbits

Yixian WEI¹⁾, Ai HORI^{1)*}, I-Ying CHEN¹⁾, Haruka TAMOGI¹⁾, Taku HIROKAWA¹⁾, Keiko KATO¹⁾, Takaharu ITAMI¹⁾, Tadashi SANO¹⁾ and Kazuto YAMASHITA¹⁾

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ABSTRACT. Recently, a mucosal atomization device (MAD) has been applied in veterinary medicine. In the present study, the maximum volume of nasal atomization without aspiration using MAD was examined in eight healthy female Japanese White (JW) rabbits. Each rabbit had their head and neck examined by computed tomography before and after nasal atomization with four different doses (0.15, 0.3, 0.45, and 0.6 ml per nostril) of diluted contrast medium (1:2 mixture of iohexol and saline). This was done under general anesthesia by an intramuscular administration of alfaxalone 2.5 mg/kg, medetomidine 40 µg/kg, and butorphanol 0.4 mg/kg, with a 7-day washout period between each treatment. The diluted contrast medium was distributed in the nasal cavity, external nares, and/or oral cavity in all rabbits receiving each treatment. The intranasal distribution volumes of the contrast medium were 287 (250–333) mm³ [median (interquartile range)] for 0.15 ml, 433 (243-555) mm³ for 0.3 ml, 552 (356-797) mm³ for 0.45 ml, and 529 (356–722) mm³ for 0.6 ml of treatment. The intranasal distribution volume for 0.15 ml treatment tended to be lower than that for 0.6 ml treatment (P=0.083). The contrast medium was deposited in the trachea in one rabbit (12.5%) and four rabbits (50%) receiving treatments of 0.45 and 0.6 ml per nostril, respectively. The maximum volume of nasal atomization without aspiration into the trachea was 0.3 ml per nostril for the JW rabbits.

KEYWORDS: intranasal administration, mucosal atomization device (MAD), nasal atomization volume, rabbit

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FULL PAPER

Internal Medicine

Evaluation of caudal vena cava size using computed tomography in dogs under general anesthesia

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ABSTRACT. This study investigated the association between caudal vena cava (CVC) size and circulatory dynamics in dogs using computed tomography (CT) under general anesthesia. The subjects were 104 dogs who had undergone CT under general anesthesia in the past. The ratio of short diameter of the CVC to aortic diameter (CVC₃/Ao) and the ratio of long to short diameter of the CVC (CVC₁/CVC₃) in the thorax and abdomen, respectively, were calculated using factors such as mean blood pressure (MBP), shock index (SI), anemia, hypoproteinemia, presence of intra-abdominal mass, and cardiac disease. There was a significant but negligible negative correlation between CVC₃/Ao and MBP. In contrast, no significant correlation was found between CVC size and SI. The low MBP group had significantly higher CVC₅/Ao of the thorax than the normal MBP group. The group with intra-abdominal mass had significantly lower CVC₅/Ao of the abdomen than the group without intra-abdominal mass. The group with cardiac disease had significantly lower CVC₁/CVC₅ of the thorax than the group without cardiac disease. In multiple regression analysis, low MBP, cardiac disease, intra-abdominal mass, and anemia were significant factors for CVC₅/Ao of the thorax, CVC₁/CVC₅ of the thorax, CVC₅/Ao of the abdomen, and CVC₁/CVC₅ of the abdomen, respectively. In conclusion, CVC size assessment using CT in dogs under general anesthesia is influenced by various factors.

KEYWORDS: caudal vena cava, computed tomography, dog, general anesthesia, hypovolemia

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Article

Evaluation of Renal Blood Flow in Dogs during Short-Term Human-Dose Epoprostenol Administration Using Pulsed Doppler and Contrast-Enhanced Ultrasonography

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Simple Summary: Since there is a lack of information regarding how epoprostenol, a prostacyclin, affects canine renal blood flow (RBF), we investigated the effects of short-term administration of epoprostenol at human doses of 2, 5, and 10 ng/kg/min intravenously for 20 min on RBF in six healthy dogs under anesthesia. The effects of short-term administration were investigated. As the dose of epoprostenol increased, peak systolic and end diastolic velocities of the renal arteries, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase. However, these increases were not significant. These results indicate that the administration of human doses of epoprostenol to dogs does not produce significant changes in renal or systemic circulation.

Abstract: Prostacyclin is an in vivo bioactive substance that regulates renal blood flow (RBF). Information regarding how epoprostenol, a prostacyclin preparation, affects RBF in dogs is lacking. We investigated the effects of short-term epoprostenol administration on RBF in six healthy dogs under anesthesia by administering it intravenously at human doses—2, 5, and 10 ng/kg/min for 20 min. RBF was evaluated before and during epoprostenol administration using pulsed Doppler ultrasonography, and renal perfusion was evaluated using contrast-enhanced ultrasonography. Effects on renal and systemic circulation were evaluated by measuring systolic arterial, mean arterial, diastolic arterial, pulmonary arterial, mean right atrial, and pulmonary capillary wedge pressures; heart rate; and cardiac output. Kruskal–Wallis and Bonferroni multiple comparison tests and Spearman's rank correlation coefficient were used for statistical analyses. As epoprostenol dosage increased, the peak systolic and end diastolic velocity of the renal artery, maximum and minimum venous flow velocities of the interlobular and renal veins, and heart rate all tended to increase, although not significantly. Our results indicate that human-dose epoprostenol administration in dogs does not cause significant changes in renal or systemic circulation. However, the human doses used may have been too low to produce a clinical effect in dogs.

Keywords: anesthesia; chronic kidney disease; contrast-enhanced ultrasonography; dog; epoprostenol; prostacyclin; pulsed Doppler ultrasonography; renal circulation

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1. Introduction

Chronic kidney disease (CKD) is fatal and causes a persistent and irreversible decline in renal function, which can lead to uremia [1,2]. In patients with CKD, further rapid decline in kidney function can occur, which is termed Acute on Chronic Kidney Disease (ACKD) [3]. Recently, there has been increasing attention on the relationship between CKD progression and interstitial lesions, and it has been reported that interstitial fibrosis, in particular, leads to CKD exacerbation and is closely related to its progression [4,5].

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NOTE

Surgery

Mid-to-caudal partial hemipelvectomy with limb preservation for ischial tumor in a dog

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ABSTRACT. A 10-year-old spayed female Golden Retriever was referred for hindlimb lameness. A firm mass was palpated over the right caudal pelvis. Computed tomography revealed an osteolytic bone region and an associated periosteal reaction in the ischium, including the acetabulum. The histological diagnosis was sarcoma of unknown origin. A mid-to-caudal partial hemipelvectomy was performed to remove the mass. Femoral head and neck osteotomy was performed to allow hindlimb preservation. Following surgery, the dog regained satisfactory hindlimb use over time and was alive for 821 days with no recurrence or metastatic disease. This report indicates that midto-caudal partial hemipelvectomy with femoral head and neck osteotomy is technically feasible and allows for tumor control with preservation of the hindlimb and its function.

KEY WORDS: dog, femoral head and neck osteotomy, limb preservation, mid-to-caudal hemipelvectomy, pelvic tumor

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FULL PAPER

Epidemiology

The impact of coronavirus disease 2019 (COVID-19) in Japanese companion animal clinics

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ABSTRACT. The coronavirus disease 2019 (COVID-19) pandemic has had a tremendous impact on people's lives throughout the world. A cross-sectional study was conducted to clarify the influence of COVID-19 on Japanese companion animal clinics. A self-administered electronic questionnaire regarding the incidence of COVID-19, hygiene management, the influence on clinical service and employment, and mental stress of staff was conducted for workers in animal clinics between 1 May and 10 June 2021. Questions concerning the hygiene management before the occurrence of COVID-19, under the first state of emergency, and at the time of the survey were asked using the Likert scale. Kessler 6 (K6) was used as an indicator of mental distress. In total, 430 individuals responded. Of these, 4.9% experienced COVID-19 infection in staff. Hygiene management was strengthened, but no particular practice was statistically associated with the occurrence of COVID-19 cases in staff. In Nakaya's variation of Scheffe's paired comparison, the highest prioritized goal in the clinics was the prevention of nosocomial infection with COVID-19. The prevalence of serious mental illness (K6 >=13) was 11.1% (95% confidence interval: 6.3-18.6%). Multivariable negative binomial regression found four risk factors for psychological distress: veterinary nurse (P=0.016 with veterinarians and P<0.01 with other staff), female (P=0.004), fear of infection at work (P<0.001), and stress by refraining from going out (P<0.001). Directors of clinics are recommended to take care of female veterinary nurses for distress.

KEYWORDS: companion animal clinic, coronavirus disease 2019, hygiene management, mental health, veterinary nurse

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Assistant Professor

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- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Measuring impact of vaccination among wildlife: The case of bait vaccine campaigns for classical swine fever epidemic among wild boar in Japan

Matsuyama R, Yamamoto T, Hayama Y, Omori R

PLOS. Comput. Biol. 18(10) e1010510. doi: 10.1371/journal.pcbi.1010510

- II. その他<Others>
 - 1) Rahman MJ, Rahman MM, <u>Matsuyama R</u>, Tsunematsu M, Islam R, Ahmed A, Banu B, Hossain SM, Sarker MHR, Monjur F, Roshid MM, Islam MR, Kakehashi M. Feasibility and acceptability of telepathology system among the rural communities of Bangladesh: A pilot study. J Family Med Prim Care. 2022;11(6):2613-9. doi: 10.4103/jfmpc.jfmpc_1876_21
- 2) Estimating the comprehensive overview of Oncorhynchus masou virus disease outbreak in Rainbow trout using mortality data: Coupling data on experimental infection and field observation by mathematical modeling.

Omori R, Matsuyama R, Nakata Y, Furihata M, Kasai H.

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Measuring impact of vaccination among wildlife: The case of bait vaccine campaigns for classical swine fever epidemic among wild boar in Japan

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Data Availability Statement: The data that support the findings of this study are available from Gifu Prefectural Government, Japan; however, the availability of data is restricted since they were used under permission of Gifu Prefectural Government, Japan, for the current study, and so

Abstract

Understanding the impact of vaccination in a host population is essential to control infectious diseases. However, the impact of bait vaccination against wildlife diseases is difficult to evaluate. The vaccination history of host animals is generally not observable in wildlife, and it is difficult to distinguish immunity by vaccination from that caused by disease infection. For these reasons, the impact of bait vaccination against classical swine fever (CSF) in wild boar inhabiting Japan has not been evaluated accurately. In this study, we aimed to estimate the impact of the bait vaccination campaign by modelling the dynamics of CSF and the vaccination process among a Japanese wild boar population. The model was designed to estimate the impact of bait vaccination despite lack of data regarding the demography and movement of wild boar. Using our model, we solved the theoretical relationship between the impact of vaccination, the time-series change in the proportion of infected wild boar, and that of immunised wild boar. Using this derived relationship, the increase in antibody prevalence against CSF because of vaccine campaigns in 2019 was estimated to be 12.1 percentage points (95% confidence interval: 7.8-16.5). Referring to previous reports on the basic reproduction number (R₀) of CSF in wild boar living outside Japan, the amount of vaccine distribution required for CSF elimination by reducing the effective reproduction number under unity was also estimated. An approximate 1.6 (when $R_0 = 1.5$, target vaccination coverage is 33.3% of total population) to 2.9 (when $R_0 = 2.5$, target vaccination coverage is 60.0% of total population) times larger amount of vaccine distribution would be required than the total amount of vaccine distribution in four vaccination campaigns in 2019.

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最終責任者 Ryosuke Omori (Corresponding Author)

Original Article

Feasibility and acceptability of telepathology system among the rural communities of Bangladesh: A pilot study

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ABSTRACT

Context: Telepathology is a promising tool for remote communities to receive pathology services where professional diagnosis services are inadequate. Aims: We aimed to clarify how effective telepathology was when compared with conventional pathology service among rural communities of Bangladesh. Methods and Materials: We conducted a cross-sectional study in suburban and rural areas of Bangladesh between June and August 2020. We enrolled 117 participants who received both telepathology services from Thakurgaon Eye Hospital and conventional pathology service experience. The participant's satisfaction with the accessibility and perceptions were statistically compared. In addition, we summarized descriptive statistics using the frequencies and percentages of participants' responses. Statistical Analysis Used: Wilcoxon's Signed-rank test using SPSS statistic software version 25.00. Results: Among the study participants, service cost, travel cost, travel time, waiting time, and travel distance were significantly higher for conventional pathology than telepathology (P < 0.001). The majority of participants (94%) were satisfied with the telepathology experience; however, one out of 117 participants was dissatisfied with this service when their travel distance was far away (≈ 50 km). Among the participants, 91.5% thought that telepathology service was effective for their treatment, and 98.3% wanted to continue this service in their community. On an average, participants saved 58% (95% CI, 53.4-61.5) of cost using telepathology rather than conventional pathology service. Conclusions: Remote under-resourced communities received professional pathology services with less time-consuming and significantly lower costs using the telepathology approach. Where pathology services are absent/insufficient, telepathology is efficacious for primary diagnosis, screening, and referral through professional pathologists for the satisfactory treatment of unreached communities.

 ${\tt Keywords: eHealth, remote communities, remote diagnosis, telepathology}$

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最終責任者 Masayuki Kakehashi (Corresponding Author)



Contents lists available at Science Direct

Aquaculture







Estimating the comprehensive overview of *Oncorhynchus masou* virus disease outbreak in Rainbow trout using mortality data: Coupling data on experimental infection and field observation by mathematical modeling

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ARTICLEINFO

Keywords: Oncorhynchus masou virus disease Salmonid herpesvirus 2 Epidemiology Basic reproduction number Experimental infection Mathematical modeling

ABSTRACT

Time series of the number of infected individuals is measured to understand the dynamics of an infectious disease and to evaluate the effectiveness of countermeasures against it. However, in fish diseases, it is often difficult to record the time series of the infected fish owing to i) ambiguous clinical symptoms during the onset of disease and ii) cost of diagnosis. To address this issue, we established a mathematical modeling-based method to infer time series of the number of infected fish by coupling the experimental infection and field data on the outbreak of the disease. This method enables to reconstruct time series of the number of infected fish using mortality data obtained from the experimental infection. The reconstructed time series enables to estimate the transmissibility of fish diseases. We studied *Oncorhynchus masou* virus (salmonid herpesvirus 2) disease (OMVD) using Rainbow trout (*Oncorhynchus mykiss*) as a model for analysis and estimated the lethality rate of OMVD infection and the basic reproduction number (R_0), i.e., transmissibility of OMVD. Our results revealed that larger fish (≥ 200 g) showed a higher OMVD lethality rate and R_0 s when compared with smaller fish (< 200 g). This suggests that high mortality among large fish does not inhibit the transmission of pathogen when compared with small fish.

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動物と人の関係学ユニット(Animal Human Relations)

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教授 郡山 尚紀

- I. 筆頭または責任著者 <First or Corresponding Author>
- 1) Yoshida, M., Miyoshi, K., Tajima, T., Wada, A., Ueda, H., & <u>Kooriyama, T.</u> Anatomical features of ossa cordis in the Steller sea lion. *Journal of Veterinary Medical Science*, 2022, 84(5), 660-665.
- 2) Satoh Y, Yoshihara K, Nakamura S, Amao A, Sasaki W, Nakanowataru Y, Sakurama M and <u>Kooriyama T.</u> Fecal Cortisol Dynamics of Captive Giraffes in Zoos in Northern, Japan International Journal of Zoology and Animal Biology, 2022, 5(3), 1-5
- II. その他<Others>



BULL PAPER

Wildlife Science

Anatomical features of ossa cordis in the Steller sea lion

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ABSTRACT. Irregular triangular cartilage or bone fragments are sometimes found in the fibrous triangle of the heart. Ossa cordis and/or cartilago cordis has been demonstrated in various terrestrial animal species. Regarding marine mammals, sperm whales lack heart bones, and there have been no studies on bones or cartilage in pinniped hearts. Therefore, we examined the ossa cordis and/or cartilago cordis of the Steller sea lion. Eleven Steller sea lion hearts were examined morphologically and histologically. Before dissection, some hearts were imaged by CT to confirm the presence of ossa cordis or cartilago cordis. As a result, ossa cordis-like fragments were confirmed in four adults and one pup. All of the fragments were found at the right fiber triangle, and one adult had ossified tissue, including adipose tissue in the bone marrow cavity. The ossa cordis probably support the aorta because they surround the aorta as in other terrestrial animals. Steller sea lions can dive to a few hundred meters, but they need to rest on land frequently. Hence, their ossa cordis help maintain heart function during the tachycardia that occurs upon repeated surfacing and movements on land after diving in water.

KEYWORDS: cardiac skeleton, cartilago cordis, ossa cordis, Steller sea lion

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Fecal Cortisol Dynamics of Captive Giraffes in Zoos in Northern Japan

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Abstract

Animals in zoos are kept under environmental conditions differing from those of their original habitat. Recently, zoos have been attempting to reduce stress by introducing environmental enrichment. Adrenal-derived glucocorticoids are common stress indicators found in blood, saliva, urine, and feces. Fecal cortisol levels have been studied as a stress marker in captive giraffes, but the data are insufficient. In this study, we examined fecal cortisol in captive giraffes in northern Japan to increase basic data on fecal cortisol as an indicator of environmental enrichment. For one month, we collected fecal samples from 14 giraffes [Masai giraffes (Giraffa camelopardalis tippelskirchi) and reticulated giraffes (Giraffa camelopardalis reticulata)] from eight zoos. The fecal samples were stored at -20 °C until fecal cortisol levels were measured using a cortisol EIA kit after drying, grinding, and ethanol extraction. Cortisol levels were compared between males and females, pregnant and nonpregnant animals, by age, and by differences in temperature of the rearing environment. The fecal cortisol levels ranged from 37~10346 pg/g. Among females, pregnant individuals had the highest values. Among nonpregnant females, a female that was harassed by a male had higher fecal cortisol levels than the others. This may be due to chronic psychological distress. In males, values varied greatly among individuals. This study increases the volume of giraffe fecal cortisol data, which will contribute to establishing basic giraffe fecal cortisol values.

Keywords: Captive; Fecal Cortisol; Giraffe; Northern Japan; Zoo

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動物と人の関係学:環境衛生 (Animal Human Relations:

Environmental Health)

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- I. 筆頭または責任著者 <First or Corresponding Author>
- Characteristics of PM_{2.5} Pollution in Osorno, Chile: Ion Chromatography and Meteorological Data
 Nakamura A, Nakatani N, Maruyama F, Fujiyoshi S, Márquez-reyes R, Fernández R, Noda J, *Atmosphere*, 13, 168, 2022. doi.org/10.3390/atmos13020168

II. その他<Others>

- 1) Maki T, Noda J, Morimoto K, Aoki K, Kurosaki Y, Huang Z, Chen B, Matsuki A, Miyata H, Mitarai S, Long-range transport of airborne bacteria over East Asia: Asian dust events carry potentially nontuberculous Mycobacterium populations, *Environment International*, 168, 107471, 2022.
- 2) Changes in CCN activity of ship exhaust particles induced by fuel sulfur content reduction and wet scrubbing
 - d. Santos L, Salo K, Kong K, Noda J, Kristensen T B, Ohigashi T, Thomson E S, *Environmental Science: Atmospheres*, 2022.





Article

Characteristics of PM2.5 Pollution in Osorno, Chile: Ion Chromatography and Meteorological Data Analyses

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Abstract: Over the decades, air pollution has become a serious problem in Osorno, Chile. This study aims to clarify the source of $PM_{2.5}$ by comprehensively analyzing its chemical composition and comparing it with meteorological conditions. The $PM_{2.5}$ and filter samples were collected during April 2019–August 2019 using a continuous particulate monitor. The analyses were conducted using Image J software, ion chromatography, and backward trajectory. The ion composition and the $PM_{2.5}$ were compared. The results on the $PM_{2.5}$ and potassium (K⁺) concentrations indicated a correlation factor of 0.93, indicating that biomass combustion, such as wood burning, is the dominant source of $PM_{2.5}$ in Osorno. High $PM_{2.5}$ concentrations of over 170 to 1124 $\mu g/m^3$ were observed in low temperature, low precipitation, and low wind speed periods—meteorological conditions contributed to the development of a thermal inversion layer. In addition, correlations of 0.61 to 0.67 were found among the detected ions that are often found in seawater. The backward trajectory analyses showed dominant air mass transport from the South Pacific Ocean, suggesting that part of the detected $PM_{2.5}$ was derived from the marine environment. Continuous monitoring and mitigation strategies focusing on wood combustion activities are necessary to alleviate the current air pollution problem in Osorno city.

Keywords: particulate matter; biomass burning; potassium ion; meteorological impact; thermal inversion layer

check for updates

Citation: Nakamura, A.; Nakatani, N.; Maruyama, F.; Fujiyoshi, S.; Márquez-Reyes, R.; Fernández, R.; Noda, J. Characteristics of PM2.5 Pollution in Osorno, Chile: Ion Chromatography and Meteorological Data Analyses. *Atmosphere* 2022, 13, 168. https://doi.org/10.3390/atmos13020168

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Full length article



Long-range transport of airborne bacteria over East Asia: Asian dust events carry potentially nontuberculous Mycobacterium populations

Teruya Maki ^{a,*}, Jun Noda ^b, Kozo Morimoto ^{c,d}, Kazuma Aoki ^e, Yasunori Kurosaki ^f, Zhongwei Huang ⁸, Bin Chen ^h, Atsushi Matsuki ¹, Hiroki Miyata ^a, Satoshi Mitarai ^b

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Keywords: Mycobacterium Nontuberculous mycobacterial pulmonary disease Asian dust Anthropogenic pollution Long-range transport Snow samples

ABSTRACT

The nontuberculous mycobacterial pulmonary disease (NTM-PD) caused by Mycobacterium species has increased in prevalence all over the world. The distributions of NTM-PD are possibly determined by the westerly wind traveling at high altitudes over East Asia. However, the long-range transport of Mycobacterium species has not been demonstrated by analyzing the bacterial communities in aerosols such as desert mineral particles and anthropogenic pollutants transported by the westerly wind. Here, airborne bacterial compositions were investigated including Mycobacterium species in high-elevation aerosols, which were captured in the snow cover at 2,450 m altitude on Mt. Tateyama. This was further compared to the ground-level or high-altitude aerosols collected at six sampling sites distributed from Asian-dust source region (Tsogt-Ovoo) to downwind areas in East Asia (Asian continental cities; Erenhot, Beijing, Yongin, Japanese cities; Yonago, Suzu, Noto Peninsula). The cell concentrations and taxonomic diversities of airborne bacteria decreased from the Asian continent to the Japan area. Terrestrial bacterial populations belonging to Firmicutes and Actinobacteria showed higher relative abundance at high-elevation and Japanese cities. Additionally, Mycobacterium species captured in the snow cover on Mt. Tateyama increased in relative abundance in correspondence to the increase of black carbon concentrations. The relative abundance of Mycobacterium sequences was higher in the aerosol samples of Asian continental cities and Japanese cities than in the desert area. Presumably, anthropogenic pollution over East Asia carries potential Mycobacterium species, which induce NTM-PD, thereby impacting upon the public health.

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最終責任者 Maki Teruya (Corresponding Authors)

Environmental Science: Atmospheres



PAPER

View Article Online



Cite this: DOI: 10.1039/d2ea00081d

Changes in CCN activity of ship exhaust particles induced by fuel sulfur content reduction and wet scrubbing?

Maritime transport remains a large source of airborne pollutants, including exhaust particles that can act as cloud condensation nuclei (CCN). While primary diesel engine exhaust particles are generally considered hydrophobic, international regulations targeting a reduction of particulate emissions from ships may have secondary effects, and therefore influence how exhaust interacts within the atmosphere. The effect of international fuel sulfur content (FSC) regulations on the cloud forming abilities of exhaust particles was investigated using a marine test engine operating on compliant low FSC fuels, non-compliant high FSC distillate fuels and in conjunction with a marine wet scrubber (fresh- and seawater). Particle sizing and liquid droplet activation measurements reveal that compliance measures can have opposing effects on the CCN activity of exhaust particles. For a non-compliant, high FSC fuel, wet scrubbing leads to an increase in CCN activity but not to significant increases in CCN emission factors. However, switching to low FSC fuels resulted in emissions of highly hydrophobic particles, causing a significant reduction in CCN activity resulting in smaller CCN emission factors by at least one order of magnitude. Our observations are supported by chemical analysis of exhaust particles using scanning transmission X-ray microscopy and near edge X-ray absorption fine structure (STXM/NEXAFS) spectra. Potential implications of effects on ship exhaust particles for cloud and climate interactions due to different compliance measures are discussed.

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Environmental significance

International marine fuel regulations are aimed at reducing emissions of airborne pollutants from the shipping sector. Using either low sulfur content fuels or alternatively high sulfur content fuels with exhaust wet scrubbers are two paths to achieving compliance that have been shown to result in unintended secondary effects on particulate matter. Here, we specifically study how these compliance alternatives affect cloud condensation nuclei (CCN) activity of fresh exhaust particles. Whereas fuel sulfur content reductions are observed to lower CCN emissions, wet scrubbing affects chemical mixing states and leads to increased emissions of more hygroscopic exhaust particles. These findings may have important implications for cloud processes and climatic feedbacks. This is of particular interest, as shipping activity is projected to increase in the Arctic, a region already subject to unprecedented anthropogenic induced climate feedbacks.

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 - 1) Expression of chemerin in intestinal mucosa of calves with comparable expressional level with other antimicrobial proteins.

Suzuki Y, Kubota K, Haga S, <u>Hayashi H</u>, Oishi M, Miura H, Roh S, Koike S, Kobayashi Y.

Anim Sci J. 93(1):e13750. 2022. DOI: 10.1111/asj.13750.

2) Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep.

Onaga T, Yasui Y, Hayashi H.

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3) Change in chemical composition and fermentation characteristics of drift seaweed during ensiling

Yamanaka M, Sanada A, <u>Hayashi H</u>, Nakagawa T, Tsukaguchi T, Hirayama T. *Journal of Animal Production Environment Science*. No.22(1). 2022. http://www.apesj.jpn.org/DL/Vol22/Yamanaka_20221107_In_Press.pdf

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RESEARCH ARTICLE



Expression of chemerin in intestinal mucosa of calves with comparable expression level with other antimicrobial proteins

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Abstract

Neonatal calves are highly susceptible to infectious disorders including diarrhea. Therefore, epithelial innate immunity, including antimicrobial peptides/proteins (AMPs), is important during the early stage of their lives. Chemerin, a multifunctional protein that was originally identified as a chemokine, possesses a potent antimicrobial activity. The present study investigated the expression levels of chemerin in the gastrointestinal (GI) tract of growing calves. Chemerin and its coding gene, retinoic acid receptor responder protein 2 (RARRES2), were highly expressed in duodenum, jejunum, and ileum compared with other parts of the GI tract. Immunohistochemistry demonstrated that chemerin-producing cells were localized in the crypt of the intestinal mucosa. Finally, the expression level of RARRES2 was higher compared with those of other major AMPs in duodenum, although it was lower compared with that of enteric β-defensin but mostly higher than those of other AMPs in jejunum and ileum at various ages in calves. The expression levels of RARRES2 were not influenced by the age of calves in duodenum and jejunum, whereas a higher expression level of RARRES2 in ileum was observed in younger calves. This study revealed that chemerin is produced in the small intestine of calves and has the potential to contribute to the gut epithelial barrier system.

KEYWORDS

antimicrobial protein, calf, chemerin, gut epithelial barrier

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Neurotensin and xenin stimulates pancreatic exocrine secretion through the peripheral cholinergic nerves in conscious sheep

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ARTICLE INFO

Keywords:
Pancreas
Enzyme
Bicarbonate
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ABSTRACT

The present study aimed to clarify the effects of neurotensin and xenin on pancreatic exocrine secretion in conscious sheep and their mechanism of actions. The animals were equipped with two silastic cannulae in the common bile duct to separately collect pancreatic fluid and bile, and a silastic cannula in the proximal duodenum to continuously return the mixed fluids. NT and xenin were intravenously injected at range of 0.01-3.0 nmol/kg during the phase I of duodenal migrating motor complex. A single intravenous NT injection significantly and dose-dependently increased pancreatic fluid, protein, and bicarbonate outputs. The effect of NT at 1 nmol/kg was completely inhibited by a background intravenous infusion of atropine methyl nitrate at a dose of 10 nmol/kg/ min, however, the effect was not altered by a prior injection of the neurotensin receptor subtype (NTR)-1 antagonist SR 48692 at 60 nmol/kg. Moreover, a single intravenous xenin-25 injection significantly and dosedependently increased pancreatic fluid and protein output, whereas the effect of xenin-25 did not clearly show dose-dependence. The prior SR 48692 injection at 30 nmol/kg did not significantly alter the effects of xenin-25 at 0.3 nmol/kg, while the atropine infusion significantly inhibited the increase in fluid secretion. Under the atropine infusion, xenin-25 at 0.3 nmol/kg did not increase protein and bicarbonate outputs, whereas the inhibitory effect of the atropine was not significant compared to that of the single injection of xenin-25. A single intravenous injection of NTR-2 agonist levocabastine at 0.1-3 nmol/kg did not alter pancreatic exocrine secretion. These results suggest that both NT and xenin-25 effectively stimulates pancreatic exocrine secretion through the peripheral cholinergic system in sheep and that NTR-2 is not involved in the regulation of pancreatic exocrine secretion, however, we did not precisely determine the role of NTR-1 in the actions of both the peptides on pancreatic exocrine secretion.

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最終責任者 Takenori Onaga (Corresponding Author)

Fermentation characteristics of drift seaweed silage

Original Paper

Change in chemical composition and fermentation characteristics of drift seaweed during ensiling

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This study considered the change in chemical composition and fermentation quality of drift seaweed

during ensiling. The drift seaweeds were pre-dried for 2 h and subsequently packed into plastic bag for 0, 15, 30 or 60 days. The moisture, ether extract, neutral detergent fiber, and non-fibrous carbohydrate content of seaweed silage

for each storage period did not differ significantly. We found positive correlations between organic acid concentrations

(acetic, propionic, lactic acids, and total organic acid) and storage duration (P < 0.001). The V-score of each ensiling

period was 100 points. These results show that drift seaweed silage can keep 60 days good fermentation condition,

and there is a possibility that it may be used as a feed resource.

Key words: Chemical composition, drift seaweed, fermentation characteristics, silage

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-319-

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 - 1) Diagnostic value of transpulmonary thermodilution measurements for acute respiratory distress syndrome in a pig model of septic shock

Endo Y, <u>Miyasho T</u>, Endo K, Kawamura Y, Miyoshi K, Takegawa R, Tagami T, Becker LB, Hayashida K.

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II. その他 <Others>

- 1) Testicular induced corticosterone synthesis in male rats under fasting stress.

 Matsuda S, Takeuchi H, Kawakubo H, Takemura R, Maeda Y, Hirata Y, Maeda N, Fujiki J, Hasegawa Y, Ieko T, <u>Miyasho T</u>, Iwasaki T, Yokota H. *Steroids*. 202; **177**: 108947. doi: 10.1016/j.steroids.2021.108947.
- 2) Early Elevation of Cell-Free DNA After Acute Mesenteric Ischemia in Rats. Karasawa S, Nakada TA, Sato M, <u>Miyasho T</u>, Shimada T, Oshima T, Suda K, Shinozaki K, Oda S.

J Surg Res. 2022; **269**: 28-35. doi: 10.1016/j.jss.2021.07.020.

RESEARCH Open Access

Diagnostic value of transpulmonary thermodilution measurements for acute respiratory distress syndrome in a pig model of septic shock



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Abstract

Background: No direct approach assessing pulmonary vascular permeability exists in the current therapeutic strategy for patients with acute respiratory distress syndrome (ARDS). Transpulmonary thermodilution measures hemodynamic parameters such as pulmonary vascular permeability index and extravascular lung water, enabling clinicians to assess ARDS severity. The aim of this study is to explore a precise transpulmonary thermodilution-based criteria for quantifying the severity of lung injury using a clinically relevant septic-ARDS pig model.

Methods: Thirteen female pigs (weight: 31 ± 2 kg) were intubated, mechanically ventilated under anesthesia, and either assigned to septic shock-induced ARDS or control group. To confirm the development of ARDS, we performed computed tomography (CT) imaging in randomly selected animals. The pulmonary vascular permeability index, extravascular lung water, and other hemodynamic parameters were consecutively measured during the development of septic lung injury. Lung status was categorized as normal (partial pressure of oxygen/fraction of inspired oxygen \geq 400), or injured at different degrees: pre-ARDS (300–400), mild-to-moderate ARDS (100–300), or severe ARDS (<100). We also measured serum inflammatory cytokines and high mobility group box 1 levels during the experiment to explore the relationship of the pulmonary vascular permeability index with these inflammatory markers.

Results: Using CT image, we verified that animals subjected to ARDS presented an extent of consolidation in bilateral gravitationally dependent gradient that expands over time, with diffuse ground-glass opacification. Further, the postmortem histopathological analysis for lung tissue identified the key features of diffuse alveolar damage in all animals subjected to ARDS. Both pulmonary vascular permeability index and extravascular lung water increased significantly, according to disease severity. Receiver operating characteristic analysis demonstrated that a cut-off value of 3.9 for the permeability index provided optimal sensitivity and specificity for predicting severe ARDS (area under the curve: 0.99, 95% confidence interval, 0.98–1.00; sensitivity = 100%, and specificity = 92.5%). The pulmonary vascular permeability index was superior in its diagnostic value than extravascular lung water. Furthermore, the pulmonary vascular

permeability index was significantly associated with multiple parameters reflecting clinicopathological changes in animals with ARDS.

Conclusion: The pulmonary vascular permeability index is an effective indicator to measure septic ARDS severity. **Keywords:** Pulmonary vascular permeability index, ARDS, Extravascular lung water, Diagnostic criteria, Large animal study.

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Testicular induced corticosterone synthesis in male rats under fasting stress

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ARTICLE INFO

Keywonis: Testicular steroidoge Testosterone Corticosterone 3β-hydroxysteroid dehydrogenase Fasting stress

ABSTRACT

Testicular steroidogenesis is depressed by adrenal-secreted corticosterone (CORT) under stress. However, the mechanisms are not well understood. This study investigated the details of testicular steroidogenesis depression during fasting. Blood levels of adrenocorticotropic hormone secreted from the pituitary glands increased, but blood CORT was not changed in rats that fasted for 96 h, in spite of the rats being severely stressed. CORT in fasting adult male rats increased more than three times in the testis, but reduced testicular testosterone (T) and blood T levels to 5% and 2% of the control, respectively, was observed. The contents of T precursor (except PGN) were drastically reduced in the insted-rat testes. Testicular CORT levels were elevated, but the enzymatic activity of cytochrome P45011β, which produces CORT, remained unchanged. The enzymatic activities of 3β-hydroxysteroid dehydrogenase (39-HSD), mediating the conversion of pregnenolone to progesterone, decreased in the fasted-rat testes. Thus, fasting suppressed testicular steroidogenesis by affecting the enzyme activity of 39-HSD in the testes and drastically reduced T and increased CORT synthesis. It can be considered that T synthesis involved in cell proliferation is suppressed due to lack of energy during fasting. Conversely, 115-hydroxylase enzyme activity was induced and CORT synthesis is increased to cope with the fasting stress. Hence, it can be concluded that CORT synthesis in the testes plays a role in the local defense response.

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Early Elevation of Cell-Free DNA After Acute Mesenteric Ischemia in Rats



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ABSTRACT

Background: Acute mesenteric ischemia (AMI) is challenging to diagnose in the early phase. We tested the hypothesis that blood levels of cell-free DNA would increase early after AMI. In addition, proteome analysis was conducted as an exploratory analysis to identify other potential diagnostic biomarkers.

Methods: Mesenteric ischemia, abdominal sepsis, and sham model were compared in Sprague-Dawley rats. The abdominal sepsis model was induced by cecum puncture and mesenteric ischemia model by ligation of the superior mesenteric artery. Blood levels of cell-free DNA were measured 2 h and 6 h after wound closure. Shotgun proteome analysis was performed using plasma samples obtained at the 2 h timepoint; quantitative analysis was conducted for proteins detected exclusively in the AMI models.

Results: Blood cell-free DNA levels at 2 h after wound closure were significantly higher in the AMI model than in the sham and the abdominal sepsis models (P < 0.05). Cell-free DNA was positively correlated with the pathologic ischemia severity score (correlation coefficient 0.793-0.834, P < 0.001). Derivative proteome analysis in blood at 2-h time point revealed higher intensity of paraoxonase-1 in the AMI models than in the abdominal sepsis models; the significantly high blood paraoxonase-1 levels in the AMI models were confirmed in a separate quantitative analysis (P = 0.015).

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