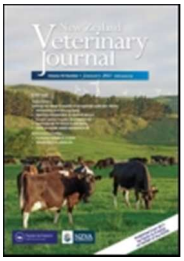

Outbreaks of anal warts containing bovine papillomavirus type 2 DNA in two mobs of heifers

Journal:	*New Zealand Veterinary Journal*
Manuscript ID	TNZV-2018-0027.R1
Manuscript Type:	Clinical Communications
Date Submitted by the Author:	n/a
Complete List of Authors:	Munday, John; Massey University School of Veterinary Science Cullum, Alison; AgResearch Ltd, Thomson, Neroli; Massey University School of Veterinary Science Bestbier, Mark; Ministry of Primary Industries McCormack, Tom; S Waikato Vet Services Julian, Alan; IDEXX
Keywords:	Anal warts, cattle, bovine papillomavirus, fibropapilloma, heifer, rectal examination, skin, BPV-2

Clinical communication

Outbreaks of anal warts containing bovine papillomavirus type 2 DNA in two mobs of heifers.

JS Munday*§, A Cullum †, NA Thomson*, M Bestbier‡, T McCormack# and AF Julian**

* Department of Pathobiology, School of Veterinary Science, Massey University, Private Bag 11 222, Palmerston North, New Zealand.
† AnexaFVC, Morrinsville, New Zealand.
‡ SVS Laboratories, Hamilton New Zealand
# South Waikato Veterinary Services, Tokoroa, New Zealand
** New Zealand Veterinary Pathology/ IDEXX Laboratories, Hamilton, New Zealand
§ Author for correspondence. Email: J.Munday@massey.ac.nz

Abstract

CASE HISTORY: Anal warts were observed in heifers in two unrelated mobs. Animals in one mob developed visible warts four months after manual rectal examination while heifers in the other mob developed warts five months after examination using a hand-held rectal probe.

CLINICAL FINDINGS: Large exophytic proliferative anal masses were observed in 5 of 15 (33%) heifers in Mob 1 and 13 of 149 (9%) heifers in Mob 2. Heifers in Mob 2 were also noted to have similar masses on the underside of the tail at sites previously used for venepuncture and some of the heifers had skin 'warts'. Despite the large size of the anal masses, none of the heifers showed clinical signs of systemic illness.

HISTOPATHOLOGICAL FINDINGS: An anal mass was removed from one heifer in each of the two mobs. Both masses were consistent with fibropapillomas and consisted of hyperplastic epithelium covering a proliferation of well-differentiated fibroblasts. Small numbers of cells within the epidermis had clear cytoplasm with clumped keratohyalin granules.

MOLECULAR BIOLOGY: Bovine papillomavirus type 2 (BPV-2) DNA was amplified from both fibropapillomas by PCR.

DIAGNOSIS: Multiple anal fibropapillomas associated with BPV-2.

CLINICAL RELEVANCE: Bovine anal warts have only been reported in heifers that have undergone rectal examination, and infection of anal microabrasions in an immunologically naïve animal appears critical for disease development. The source and method of spread of BPV-2 within these mobs could not be determined. However, spread of BPV-2 within the mobs by the veterinarian performing rectal examinations may have been most likely. While these warts had a dramatic appearance, like warts elsewhere on the body, they did not have any significant effect on the health of the affected heifers. As these lesions can be diagnosed by clinical examination and self-resolve without treatment, it is important that veterinarians are aware of this rare manifestation of papillomavirus infection of cattle.

KEY WORDS: *Anal warts, cattle, bovine papillomavirus, heifer, fibropapilloma, rectal examination, skin.*

BPV Bovine papillomavirus

Introduction

The most frequently observed manifestation of papillomavirus infection of cattle is the development of a hyperplastic 'wart' on the skin or within the upper alimentary tract. Such lesions are subdivided into papillomas, that are formed by a proliferation of the epithelium, and fibropapillomas that contain proliferations of epithelial cells and fibroblasts within the underlying tissue (Munday 2014). Papillomavirus infection is common in cattle and most cattle will develop warts during their lives (Lindholm *et al* 1984). Currently, 23 different bovine papillomavirus (BPV) types have been fully sequenced and subdivided into five genera (Munday *et al* 2015b; Daudt *et al* 2016). One of the more common BPV types to be detected in cattle is BPV-2 and this papillomavirus can asymptomatically infect cattle as well as cause cutaneous, genital, and upper alimentary tract fibropapillomas (Borzacchiello *et al* 2003; Munday 2014). BPV-2 has also been associated with bladder neoplasia (Borzacchiello

and Roperto 2008; Roperto *et al* 2016) although these cancers are highly dependent on concurrent exposure to carcinogens in bracken fern. As bracken fern in New Zealand tends to have low levels of carcinogens (Rasmussen *et al* 2008) such cancers are rarely observed in cattle in New Zealand.

Papillomaviruses cause disease by stimulating epithelial cell replication (Munday 2014). If the host is able to prevent papillomavirus-induced cell replication then the infection will be asymptomatic. However, infection of an immunologically naïve animal can result in marked papillomavirus-induced cell replication and the development of a visible papilloma or fibropapilloma. The immune response to infection by a papillomavirus includes a humoral response and a cell-mediated response. The humoral response prevents further infections by the papillomavirus type, but does not influence the resolution of the current infection (Kirnbauer *et al* 1996). Resolution of a current infection is dependent on the cell-mediated response (Egawa and Doorbar 2017). As the time taken to initiate this response is variable, there can be significant variation in the time that warts are present prior to spontaneous regression (Olson *et al* 1992). However, warts in almost all cattle will resolve within 12 months and after resolution the animal is protected against the development of further warts caused by this papillomavirus type.

Papillomaviruses can be spread by direct contact or by indirect spread from farming equipment or the environment (Munday and Pasavento 2017). For a papillomavirus infection to occur, epithelial microabrasions are required to allow the virus access to basal cells (Doorbar *et al* 2012). Warts in cattle most frequently develop around the head and neck, teats, and genitals and this distribution may reflect the places on the body where microabrasions are most likely to occur. As warts only develop the first time that infection with a BPV type occurs, they typically develop in young animals.

The present report describes two unrelated mobs of heifers in which multiple animals developed anal fibropapillomas. By using molecular techniques it was possible to identify BPV-2 DNA sequences within the fibropapillomas. This is the second report of anal warts in cattle and the first report of this disease in cattle from New Zealand.

Case History

Mob 1. This mob comprised 15 Friesian cross heifers which had been first run with a bull eight months prior to presentation. The bull was removed after 1 month and three months

later the heifers were pregnancy tested by manual rectal examination. The heifers were considered by the veterinarian to be small for their age. Four months after rectal examination, large proliferative masses around the anus were observed in five animals. These lesions were initially non-ulcerated; however, the masses became reddened and ulcerated after the farmer cleaned them using a stiff brush.

Mob 2. This mob comprised 140 Friesian cross heifers. As part of a research study, they underwent an examination using a hand-held rectal ultrasound probe. Due to the small size of the animals, significant rectal stretching was noted in many of the heifers. A blood sample was also taken from the tail vein at the same time. Bulls were introduced to the mob two months after the ultrasound procedure. Five months after the rectal examination, multiple animals were observed to have anal masses.

The heifers in the two mobs came from unrelated sources, were geographically separated, and were attended by different veterinarians.

Clinical Findings

Mob 1. Examination confirmed that 5 of 15 (33%) heifers had multiple 1 - 10 cm diameter exophytic anal masses. The masses often appeared vegetative and had a roughened surface. Most masses were within the non-haired skin of the anus, although occasional extension into the haired skin surrounding the anus was present. In some animals, the masses formed a coalescing multilobular circumferential ring surrounding the anus (Figure 1). Involvement of the vulva was not observed in any of the heifers and warts were not observed elsewhere on the body. The masses were reddened and ulcerated and often had significant faecal contamination. The affected cattle were in good body condition and did not show any other clinical signs of disease. One of the masses was excised under local anaesthetic using a scalpel blade and fixed in formalin. The mass was noted to have a firm texture on excision.

All of the heifers in the mob calved routinely within a month of the samples being taken and all subsequently milked normally. Evaluation three months later revealed that the masses had almost completely resolved; however, all five affected cattle had residual poorly-defined nodular thickening in the skin of the anal region.

Mob 2. Examination of the 140 heifers revealed that 28 had warts. This number included 13 (9%) animals that had nodular proliferative masses within the anal region. These masses were typically multiple, 0.5 - 10 cm in diameter, non-ulcerated, and often coalesced into large multilobular masses. Three heifers had nodular proliferative masses that were restricted to the

underside of the tail in a place that was interpreted to be the site of venepuncture. These masses were smaller and fewer in number than the anal masses. One heifer had anal masses and a single nodular mass at the venepuncture site (Figure 2). Twelve heifers had proliferative masses that were restricted to the head and neck while one heifer had masses both on the skin and around the anus. A sample of an anal mass was taken from one heifer under local anaesthetic and fixed in formalin.

The mob was re-examined four months later. At this time, anal warts were still visible in two animals. However, warts in both heifers were observed to be harder on palpation and notably smaller than they had been four months previously. None of the animals had skin or tail warts at this time. All animals in the mob were otherwise healthy.

Pathological and Laboratory Findings

Formalin fixed samples were embedded in paraffin, sectioned, and stained with haematoxylin and eosin for histopathology. Both submitted masses appeared as circumscribed proliferations of mesenchymal cells arranged in loose bundles and whorls within the submucosa. The mesenchymal proliferations were covered by thickened epithelium that formed prominent thin rete pegs that extended into the underlying submucosa (Figure 3). The thickened epithelium of both masses contained small clusters of keratinocytes that were enlarged by increased quantities of clear cytoplasm with a centrally-placed pyknotic nucleus. Additionally, cells within the superficial layers of the epithelium had prominent nuclei that were surrounded by clumped keratohyalin granules (Figure 4). The epithelium was covered by increased quantities of predominantly orthokeratotic keratin. The underlying submucosa of both masses was expanded by a well-differentiated population of spindle-shaped cells that had indistinct cell borders. The cells had large prominent centrally-placed elongate nuclei that often had prominent multiple nucleoli and large quantities of lightly eosinophilic vacuolated cytoplasm. Both masses contained multiple foci of predominantly lymphoplasmacytic inflammation scattered within the expanded submucosa. The mass removed from the heifer from Mob 1 was partially ulcerated and the ulcerated areas were covered by a thin zone of necrosis and degenerate and non-degenerate neutrophils. The mass from the heifer from Mob 2 was covered by intact epithelium. Both masses were diagnosed as fibropapillomas.

To investigate a possible papillomavirus aetiology, total DNA was extracted from formalin-fixed paraffin-embedded sections of both fibropapillomas as previously described (Munday *et al* 2007). The FAP59/64, MY09/11 and CP4/5 consensus PCR primers were then used to

amplify DNA from as wide a range of papillomavirus types as possible (Munday *et al*
159 2015a). Positive controls were DNA extracted from a canine oral papilloma containing canine papillomavirus 1 for FAP59/64 and DNA extracted from a feline sarcoid containing BPV-14 for the MY09/11 and CP4/5 primers. No template DNA was added to the negative
162 controls. Amplicons of the expected sizes were amplified from the positive control reactions and no DNA was amplified from the negative controls. Amplicons of the expected size were amplified from both fibropapillomas using the FAP59/64 and CP4/5 primers, but from
165 neither sample using the MY09/11 primers. DNA was purified as previously described (Munday *et al* 2017) and compared to known sequences in GenBank. The DNA that was amplified by both sets of consensus primers from both fibropapillomas was found to be
168 identical to that of BPV-2. The failure of the FAP59/64 primers to amplify DNA from other PV types suggests that BPV-2 was the only PV type present within the fibropapillomas.

171 **Discussion**

Anal fibropapillomas (warts) were diagnosed using histopathology in heifers from two unrelated mobs of cattle in New Zealand. Anal warts in cattle have only been reported once
174 previously when an outbreak was described in a herd of beef cattle in Australia (Tweddle and White 1977). In the presently-described cases, the anal warts appeared as exophytic, bulging, hairless masses. The majority of the masses were non-ulcerated, although as observed in the
177 wart from Mob 1, trauma can damage the overlying epithelium resulting in partial ulceration and potentially secondary infection. While the diagnosis of fibropapillomas was made by histopathology in both currently reported cases, greater awareness of the development of
180 these warts should enable a clinical diagnosis to be made as there are no differential diagnoses for exophytic anal masses affecting multiple animals in a mob. The recognition of anal warts is important as, despite their considerable size, they are expected to spontaneously
183 resolve and not significantly affect the health of the animal.

Fibropapillomas from both mobs were found to contain BPV-2 DNA. This is the first time that the papillomavirus type within anal warts in cattle has been determined. BPV-2 is a
186 *Deltapapillomavirus* and is thought to be a common cause of fibropapillomas of the skin and genitals of cattle (Munday 2014). The detection of only this virus type in both fibropapillomas suggests that it was likely to be the cause of the warts. However,
189 papillomaviruses commonly asymptomatically infect cattle skin (Ogawa *et al* 2004) and

warts can contain multiple BPV types (Schmitt *et al* 2010). Therefore, it remains possible that BPV-2 was detected as an incidental infection in the fibropapilloma and the causative papillomavirus was not amplified by any of the three sets of consensus primers used. If BPV-2 was the cause of the anal fibropapillomas, this suggests that the rarity of these lesions is not because they are caused by an unusual papillomavirus type, but rather because of an unusual route or timing of infection by a common papillomavirus type.

Cattle in the present report and in the previous Australian report all had a history of rectal examination prior to the development of anal fibropapillomas (Tweddle and White 1977). In the presently-reported cattle, the rectal examination occurred between four and five months prior to the warts being observed while rectal examination occurred three months before warts developed in the Australian cases. Rectal examination probably predisposes to anal warts by causing microabrasions of the anus. It is interesting that animals in both presently reported mobs were described as small suggesting greater than normal anal microabrasion could have occurred due to rectal examination. While rectal examination appears to be necessary for the development of the warts, it should be noted that many cattle in New Zealand, undergo rectal examination, but very few of them develop anal warts. Therefore, factors in addition to rectal examination are required for the development of the disease.

Currently, bovine anal warts have only been described in heifers. While heifers may be predisposed to greater anal microabrasion during rectal examination, it is likely that heifers are also predisposed to anal warts as they are less likely to have been previously infected by the causative papillomavirus type. The first time that an animal is infected by a papillomavirus type, this infection may cause wart development. However, subsequent exposure to the papillomavirus type will not result in visible disease (Campo 1997). In the presently described heifers it therefore appears that the animals were initially infected by BPV-2 around the time of rectal examination. The infection of the anal microabrasions by a papillomavirus type to which the heifers were immunologically naïve, allowed the development of the florid anal warts. The hypothesis that the heifers were first infected by BPV-2 around the time of rectal examination is supported by the observation that heifers in Mob 2 developed both skin and anal warts suggesting papillomaviruses infected anal microabrasions in some animals and skin microabrasions in others, but many of the heifers in this mob had not been previously infected by the causative papillomavirus type.

The cause of the anal warts in the present cases cannot be definitively determined. However, it appears most likely that the process of rectal examination by the veterinarians could have

been a key process. The veterinarians could have contributed to the outbreak by using contaminated equipment that introduced BPV-2 to the mob and directly infected the cattle during rectal examination. This could happen, for example, if the lubricant, gloves, or ultrasound probe used during the examinations had been previously contaminated by BPV-2. This appears possible because papillomaviruses are resistant in the environment and indirect spread of papillomaviruses by fomites is well recognised (Munday and Pasavento 2017). Additionally, even if the veterinarians did not introduce BPV-2 into the mobs, it is possible that the veterinarians could have caused the outbreaks of warts by transmitting BPV-2 between animals while performing the rectal examination. This could occur if the gloves used became contaminated with BPV-2 from a pre-existing cutaneous or genital wart that was present in one of the heifers in each mob. By using gloves contaminated by infectious viral particles, the papillomaviruses could then have been directly transmitted into the anal microabrasions that developed during rectal examination. If one heifer in the mob was infected by BPV-2, but the others were immunologically naïve to this papillomavirus type, transmission of the virus within the mob during rectal examination could explain the development of the anal warts. While inoculation of anal microabrasions by the veterinarian appears to be the most likely cause of the warts, why anal warts appear to be so rare in cattle is uncertain. It is possible that significant equipment contamination occurs rarely. Alternatively, if the veterinarians' gloves were contaminated by contact with a wart, the unusual feature in the present mobs may have been presence of a wart in one animal while the remainder of the animals in the mob remained immunologically naïve.

Alternatively, it cannot be excluded that introduction of the bulls could have been the key factor as these could have been infected by BPV-2 and their mating behavior subsequently infected the anal microabrasions caused by rectal examination. However, bulls were not introduced to Mob 2 until six weeks after rectal examination. Therefore, for the bulls to have caused the anal warts, anal microabrasions due to rectal examination would have had to persist for six weeks. Likewise, as heifers in Mob 2 also developed warts at the site of venepuncture, the traumatic lesions caused by venepuncture would also have had to persist for six weeks. It seems unlikely that either rectal examination or venepuncture could result in such significant damage that the skin would not have been fully repaired within six weeks.

Four heifers in Mob 2 developed fibropapillomas that were interpreted to be at the site of blood sampling. This localization of warts at the venepuncture sites suggests that skin trauma caused by blood sampling allowed papillomavirus infection. Warts can develop secondary to

tattooing in people suggesting that needles can facilitate papillomavirus infection of the skin (Wanat *et al* 2014).

In the Australian report, around half of the heifers in the mob developed anal warts. In comparison warts were seen in 9% and 33% of the heifers in the presently-described mobs. The reason for the lower rates of wart development in the affected mobs in New Zealand is uncertain. However, if the papillomavirus was spread from one to multiple animals in the mob by the veterinarian, the lower incidence in New Zealand could have been because the veterinarian became contaminated by BPV-2 later in the course of the examinations so that a smaller proportion of animals in the New Zealand mobs were exposed to the papillomavirus. Alternatively, it is possible that a smaller proportion of heifers in New Zealand developed warts because the veterinarians in New Zealand caused anal microabrasions in a smaller proportion of cattle.

Available evidence suggests that bovine anal warts are caused by a combination of anal trauma and exposure of immunologically naïve animals to the papillomavirus. Therefore, to prevent anal warts from developing, ensuring adequately lubrication to minimise anal trauma is advisable. Alternatively, it may be possible to deliberately expose cattle to papillomavirus infection earlier in life. Therefore, when animals subsequently undergo rectal examinations, the presence of humoral antibodies will prevent the development of anal warts. Vaccination with virus-like particle vaccines would be expected to be a safe and effective preventative, although currently no vaccines are commercially available. As it appears likely the veterinarian performing the rectal examination could transmit the papillomavirus between animals, frequent glove changes could be beneficial, especially when performing rectal examinations on mobs of heifers that are more likely not to have been previously infected by papillomaviruses.

As expected, the anal warts in both mobs resolved over a period of three to six months. Unexpectedly, some animals were left with mild residual nodular thickening of the anus. This residual thickening may be fibrosis that developed as a result of secondary bacterial infection of the warts rather than representing any residual wart tissue. Currently there are no proven treatments that accelerate the resolution of warts in cattle. Crushing of warts or injecting inactivated extracts of warts (autologous vaccines) has not been proven to be effective. While a variety of other treatments have been reported to hasten lesion regression of warts in cattle in small pilot studies (Hemmatzadeh *et al* 2003; Borku *et al* 2007), larger controlled studies

of these potential treatments are lacking. Symptomatic therapy to prevent secondary bacterial infection or for pain relief should be considered for animals with warts that become ulcerated.

In conclusion, outbreaks of anal fibropapillomas that were most likely caused by BPV-2 developed in mobs of heifers. Anal warts developed in both mobs within a few months of rectal examination. The lesions had a characteristic clinical appearance. As none of the affected animals showed signs of systemic illness due to the warts and all warts eventually spontaneously resolved, veterinarians should be aware of the possibility of these lesions so that appropriate advice can be given. While these lesions could be prevented by ensuring all animals have been exposed to papillomaviruses prior to rectal examination, the low significance of these fibropapillomas suggests management changes to prevent them may not be necessary.

References

Borku MK, Atalay O, Kibar M, Cam Y, Atasever A. Ivermectin is an effective treatment for bovine cutaneous papillomatosis. *Research in Veterinary Science* 83, 360-3, 2007

Borzacchiello G, Iovane G, Marcante ML, Poggiali F, Roperto F, Roperto S, Venuti A. Presence of bovine papillomavirus type 2 DNA and expression of the viral oncoprotein E5 in naturally occurring urinary bladder tumours in cows. *The Journal of General Virology* 84, 2921-6, 2003

Borzacchiello G, Roperto F. Bovine papillomaviruses, papillomas and cancer in cattle. *Veterinary Research* 39, 45, 2008

Campo MS. Vaccination against papillomavirus in cattle. *Clinics in Dermatology* 15, 275-83, 1997

Daudt C, da Silva FRC, Streck AF, Weber MN, Mayer FQ, Cibulski SP, Canal CW. How many papillomavirus species can go undetected in papilloma lesions? *Scientific Reports* 6, 36480, 2016

Doorbar J, Quint W, Banks L, Bravo IG, Stoler M, Broker TR, Stanley MA. The biology and life-cycle of human papillomaviruses. *Vaccine* 30, F55-70, 2012

Egawa N, Doorbar J. The Low-Risk Papillomaviruses. *Virus Research* 231, 119-27, 2017

Hemmatzadeh F, Fatemi A, Amini F. Therapeutic effects of fig tree latex on bovine papillomatosis. *Journal of Veterinary Medicine, Series B* 50, 473-6, 2003

Kirnbauer R, Chandrachud LM, O'Neil BW, Wagner ER, Grindlay GJ, Armstrong A, McGarvie GM, Schiller JT, Lowy DR, Campo MS. Virus-like particles of bovine papillomavirus type 4 in prophylactic and therapeutic immunization. *Virology* 219, 37-44, 1996

Lindholm I, Murphy J, O'Neil BW, Campo MS, Jarrett WF. Papillomas of the teats and udder of cattle and their causal viruses. *The Veterinary Record* 115, 574-7, 1984

Munday JS, Kiupel M, French AF, Howe L, Squires RA. Detection of papillomaviral sequences in feline Bowenoid in situ carcinoma using consensus primers. *Veterinary Dermatology* 18, 241-5, 2007

Munday JS. Bovine and human papillomaviruses: A comparative review. *Veterinary Pathology* 51, 1063-75, 2014

Munday JS, Fairley RA, Mills H, Kiupel M, Vaatstra BL. Oral papillomas associated with Felis catus papillomavirus type 1 in 2 domestic cats. *Veterinary Pathology* 52, 1187-90, 2015a

Munday JS, Thomson N, Dunowska M, Knight CG, Laurie RE, Hills S. Genomic characterisation of the feline sarcoid-associated papillomavirus and proposed classification as Bos taurus papillomavirus type 14. *Veterinary Microbiology* 177, 289-95, 2015b

Munday JS, Marshall S, Thomson NA, Kiupel M, Heathcott RW, French A. Multiple viral plaques with sebaceous differentiation associated with an unclassified papillomavirus type in a cat. *New Zealand Veterinary Journal* 65, 219-223, 2017

***Munday JS, Pasavento P.** Papillomaviridae and Polyomaviridae. In: MacLachlan NJ, Dubovi EJ (eds). *Fenner's Veterinary Virology*. Pp 229-43. Academic Press, London, United Kingdom, 2017

Ogawa T, Tomita Y, Okada M, Shinozaki K, Kubonoya H, Kaiho I, Shirasawa H. Broad-spectrum detection of papillomaviruses in bovine teat papillomas and healthy teat skin. *The Journal of General Virology* 85, 2191-7, 2004

Olson C, Olson RO, Hubbard-Van Stelle S. Variations of response of cattle to experimentally induced viral papillomatosis. *Journal of the American Veterinary Medical Association* 201, 56-62, 1992

Rasmussen L, Lauren D, Smith B, Hansen H. Variation in ptaquiloside content In bracken (Pteridium esculentum (Forst. f) Cockayne) in New Zealand. *New Zealand Veterinary Journal* 56, 304-9, 2008

Roperto S, Munday JS, Corrado F, Goria M, Roperto F. Detection of bovine papillomavirus type 14 DNA sequences in urinary bladder tumors in cattle. *Veterinary Microbiology* 190, 1-4, 2016

Schmitt M, Fiedler V, Muller M. Prevalence of BPV genotypes in a German cowshed determined by a novel multiplex BPV genotyping assay. *Journal of Virological Methods* 170, 67-72, 2010

Tweddle NE, White WE. An outbreak of anal fibropapillomatosis in cows following rectal examinations. *Australian Veterinary Journal* 53, 492-5, 1977

Wanat KA, Tyring S, Rady P, Kovarik CL. Human papillomavirus type 27 associated with multiple verruca within a tattoo: report of a case and review of the literature. *International Journal of Dermatology* 53, 882-4, 2014

Figure legends

Figure 1. Heifer from Mob 1. The anal fibropapillomas are exophytic proliferative masses that often coalesce into large multilobular masses. The fibropapillomas have formed a circumferential mass that is restricted to the non-haired skin of the anus.

Figure 2. Heifer from Mob 2. The anal fibropapillomas are visible as exophytic proliferative masses involving the ventral half of the anus. Close to the top of the figure is a smaller mass that developed at the site of venepuncture.

Figure 3. Photomicrograph of sections of an anal wart from a heifer from Mob 2. Hyperplastic epithelium is present overlying a proliferation of short spindle-shaped cells within the submucosa. Numerous thin rete pegs are visible extending from the epithelium into the underlying proliferating mesenchymal cells. H&E. Bar = 0.2 mm.

Figure 4. Photomicrograph of sections of an anal wart from a heifer from Mob 2. The epithelium contains small numbers of cells that have increased quantities of non-staining cytoplasm and a central dark shrunken nucleus. Clumping of keratohyalin granules is also visible (arrows). H&E. Bar = 22 µm.

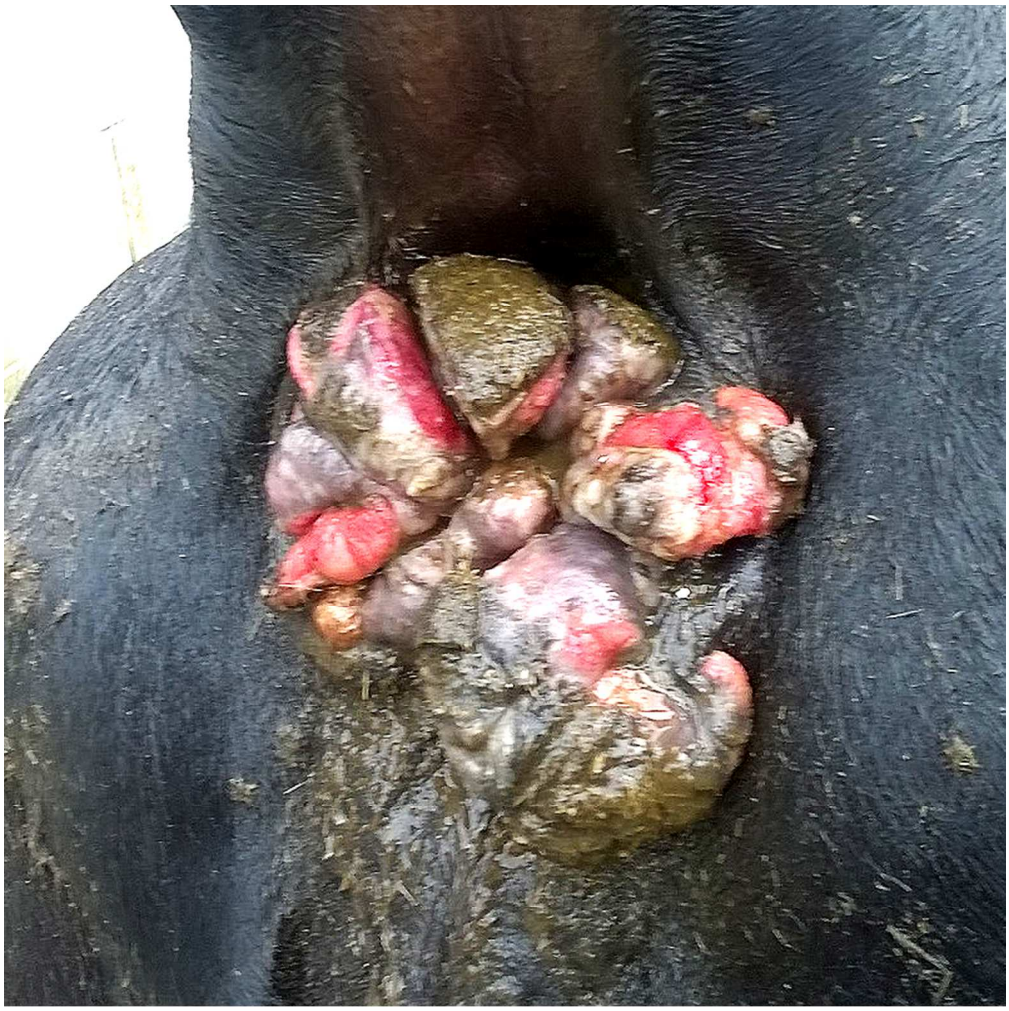

Figure 1. Heifer from Mob 1. The anal fibropapillomas are exophytic proliferative masses that often coalesce into large multilobular masses. The fibropapillomas have formed a circumferential mass that is restricted to the non-haired skin of the anus.

90x90mm (300 x 300 DPI)

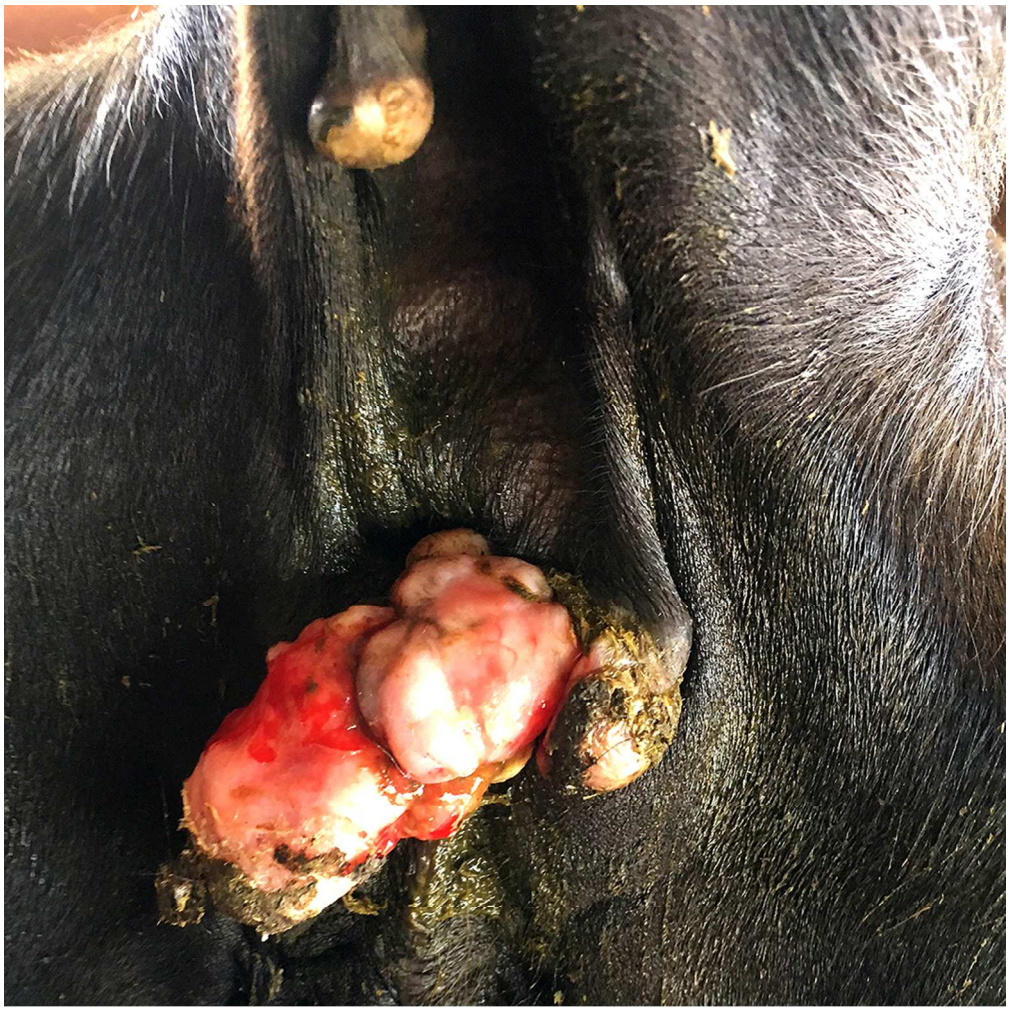

Figure 2. Heifer from Mob 2. The anal fibropapillomas are visible as exophytic proliferative masses involving the ventral half of the anus. Close to the top of the figure is a smaller mass that developed at the site of venepuncture.

90x90mm (300 x 300 DPI)

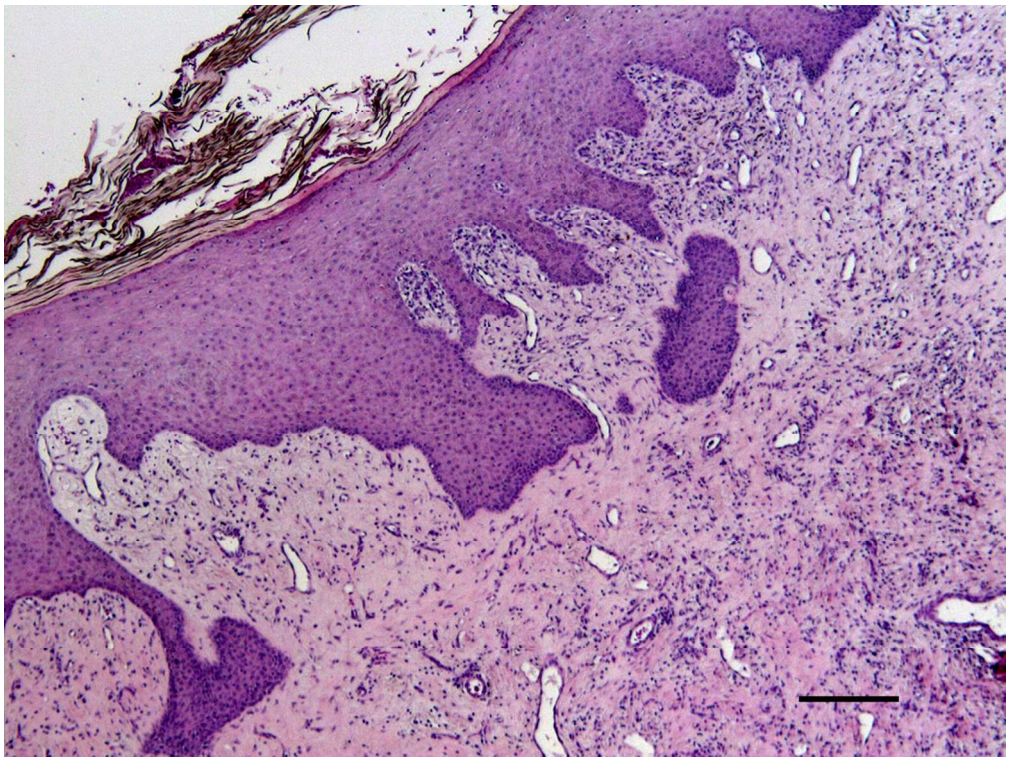

Figure 3. Photomicrograph of sections of an anal wart from a heifer from Mob 2. Hyperplastic epithelium is present overlying a proliferation of short spindle-shaped cells within the submucosa. Numerous thin rete pegs are visible extending from the epithelium into the underlying proliferating mesenchymal cells. H&E. Bar = 0.2 mm.

90x67mm (300 x 300 DPI)

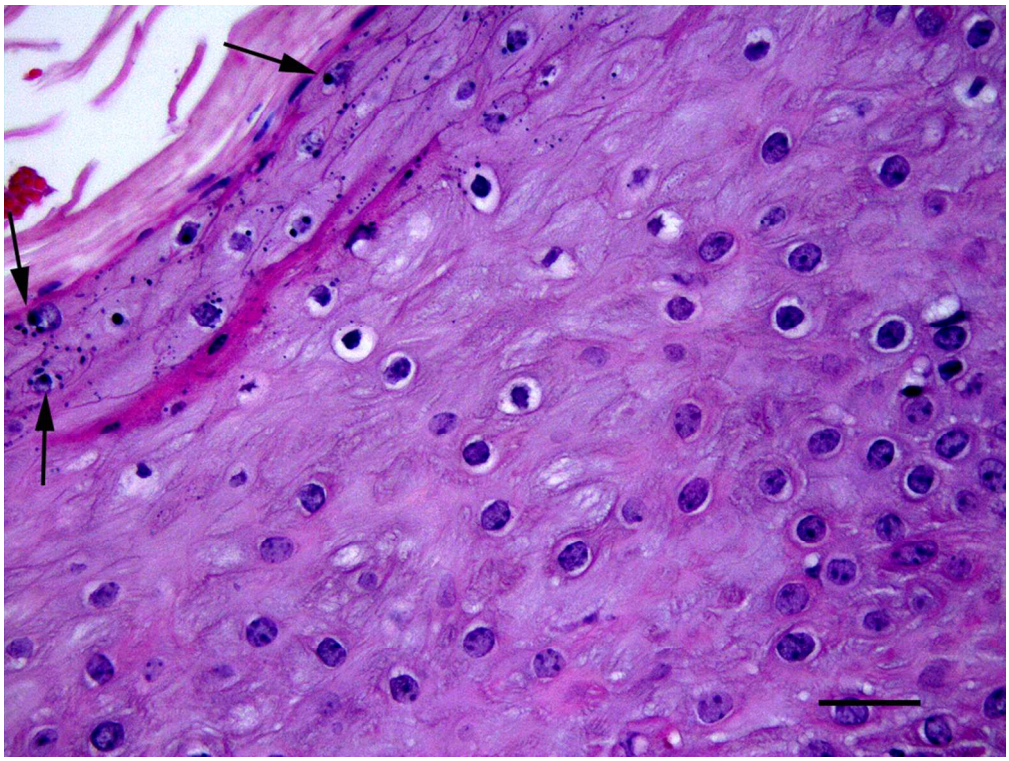

Figure 4. Photomicrograph of sections of an anal wart from a heifer from Mob 2. The epithelium contains small numbers of cells that have increased quantities of non-staining cytoplasm and a central dark shrunken nucleus. Clumping of keratohyalin granules is also visible (arrows). H&E. Bar = 22 µm.

90x67mm (300 x 300 DPI)