

Sheep Pox and Goat Pox

*Capripoxvirus Infections,
Capripox*

Last Updated: August 2017



IOWA STATE UNIVERSITY
College of Veterinary Medicine



Importance

Sheep pox and goat pox are contagious viral diseases of small ruminants. These diseases may be mild in indigenous breeds living in endemic areas, but they are often fatal in newly introduced animals. Economic losses result from decreased milk production, damage to the quality of hides and wool, and other production losses. Sheep pox and goat pox can limit trade, inhibit the development of intensive livestock production, and prevent new breeds of sheep or goats from being imported into endemic regions.

Etiology

Sheep pox and goat pox result from infection by sheeppox virus (SPPV) or goatpox virus (GTPV), closely related members of the genus *Capripoxvirus* in the family Poxviridae. SPPV is mainly thought to affect sheep and GTPV primarily to affect goats, but some isolates can cause mild to serious disease in both species. SPPV and GTPV can be distinguished by a few specialized genetic tests. These tests are not widely available, and isolates are typically assigned to SPPV or GTPV based on the animal species affected during an outbreak. However, some studies suggest that this assumption is not always valid.

SPPV and GTPV are closely related to lumpy skin disease virus (LSDV), a capripoxvirus that affects cattle. These three viruses cannot be distinguished by many diagnostic tests, including all tests that detect antibodies or viral antigens.

Species Affected

SPPV and GTPV only appear to affect sheep and goats. It seems plausible that these viruses could cause disease in wild relatives of small ruminants, but there are no reports of any infections in free-living or captive wild species. Antibodies to capripoxviruses have been reported in some wild ungulates, but these studies were conducted in southern Africa, where SPPV and GTPV appear to be absent. In Saudi Arabia, a putative clinical case in an Arabian oryx (*Oryx leucoryx*) was diagnosed by methods that cannot distinguish LSDV from other capripoxviruses. However, the illness appeared to resemble lumpy skin disease (LSD) rather than sheep pox or goat pox, and it was identified as LSD.

Zoonotic potential

SPPV and GTPV are not thought to infect humans. Two published cases suggested that capripoxviruses might be transmitted to people, but these reports are considered doubtful.

Geographic Distribution

Sheep pox and goat pox are endemic in north and central Africa, parts of the Middle East, Turkey, and some parts of Asia including the Indian subcontinent. Frequent outbreaks in Greece and occasional outbreaks in Bulgaria are thought to be caused by viruses that enter these countries during outbreaks in Turkey.

Transmission

SPPV and GTPV appear to be transmitted mainly during close contact, but also occur in contaminated environments. Aerosols are thought to be important in transmission. These viruses may also enter the body through other mucous membranes or abraded skin. SPPV and GTPV are shed in saliva, nasal and conjunctival secretions. They are also abundant in skin lesions and their scabs, and viruses have been detected in milk, urine, feces and semen. Animals are most contagious during the first week after the onset of clinical signs, but some experimentally infected sheep and goats continued to shed smaller amounts of virus in nasal, conjunctival and oral secretions for 1-2 months. One article mentions that the authors have seen vertical transmission in small ruminants, but there are no details. Sheep and goats do not become chronically infected carriers.

Mechanical transmission by insects appears possible, although it is not thought to be important in the epidemiology of sheep pox or goat pox. Stable flies (*Stomoxys calcitrans*) were demonstrated to transmit SPPV and GTPV mechanically in the

laboratory, but biting lice (*Mallophaga* spp.), sucking lice (*Damalinia* spp.), sheep head flies (*Hydrotaea irritans*) and midges (*Culicoides nubeculosus*) did not infect naive animals. However, SPPV was found in sheep head flies that had fed on infected sheep.

SPPV and GTPV may remain viable for prolonged periods in the environment, making transmission possible on fomites. These viruses are thought to persist for up to 6 months if they are protected from the environment, as in shaded, uncleaned sheep pens. They may also be found for at least a few months in dry scabs, fleeces and hair. Poxviruses are resistant to drying, and they can survive freeze/thaw cycles, although their infectivity may be reduced.

Disinfection

Capripoxviruses are susceptible to a number of disinfectants including sodium hypochlorite, iodine, quaternary ammonium agents, ether, chloroform, formalin, phenol, and detergents that contain lipid solvents. Highly alkaline or acid conditions (2% hydrochloric or sulfuric acid) are also reported to be effective.

Capripoxviruses are reported to be destroyed by heating to 56°C (133°F) for 2 hours, or to 65°C (149°F) for 30 minutes. Some studies reported that holding capripoxviruses at 56°C for one hour inactivated them, but other reports, which used different strains, found that this treatment did not significantly reduce viral titers.

Incubation Period

Estimates of the incubation period in the field differ between sources, but are generally in the range of 1-2 weeks. Clinical signs would be expected to appear sooner when the virus is inoculated by insects than when it is transmitted in aerosols. After experimental inoculation into the dermis, primary lesions can develop at the site within 2-4 days.

Clinical Signs

Sheep pox and goat pox appear similar, with clinical signs that typically include fever, enlarged superficial lymph nodes, oculonasal discharge, and poxviral lesions that may affect the skin, mucous membranes and internal organs. Some animals develop numerous lesions and become severely ill; others have mild or no clinical signs.

Skin lesions tend to be more frequent and visible on sparsely woolled/ haired skin such as the axillae, muzzle, eyelids, ears, mammary gland and inguinal area, but in more severe cases, they may cover the entire body. In animals with heavy wool, lesions can be easier to find by palpation than visual inspection. Some animals may have only a few lesions, often around the ears or the tail. Skin lesions typically begin as erythematous macules and develop into 0.5-1.5 cm hard papules. The centers of the papules become depressed, whitish gray and necrotic, and are surrounded by an area of hyperemia. They eventually develop dark, hard, sharply demarcated scabs. Vesicles might be seen during the

intermediate stage, but are uncommon. The older literature also describes a nodular form of sheep and goat pox ('stonepox') that resembles lumpy skin disease of cattle, with nodules that extend through the full thickness of the skin. These nodules eventually become necrotic and slough, leaving a hairless scar. Other descriptions of sheep and goat pox mention typical pox-like lesions and nodules in the same animal. A highly fatal, flat hemorrhagic form of goat pox, with papules that seem to coalesce over the body, has been reported in European breeds of goats.

Mucosal lesions can develop at various sites including the mouth, nares, eyes, anus, vagina and prepuce. These lesions tend to ulcerate or become necrotic. Oral and nasal lesions can cause inappetence, rhinitis and excessive salivation, with discharges that eventually become mucopurulent. Papules on the eyelids and ocular lesions can result in blepharitis and conjunctivitis. Other signs vary, depending on the internal organs affected, but can include depression, as well as coughing and dyspnea (lesions affecting the lungs), diarrhea (lesions in the intestinal tract), and emaciation. Some animals may abort.

Animals can die at any stage of the illness, occasionally even before the appearance of the characteristic external lesions. Surviving animals recover at varying rates, and recovery can be slow in severe cases. Skin lesions can take several weeks to heal, and they may leave permanent scars. Complications can include fly strike and secondary bacterial infections, including pneumonia.

Post Mortem Lesions [Click to view images](#)

The skin usually contains macules, papules and/or necrotic lesions and scabs, surrounded by areas of edema, hemorrhage and congestion. The papules penetrate through both the dermis and epidermis; in severe cases, they may extend into the musculature. Skin lesions may not be as apparent at necropsy as they are in living animals. The mucous membranes of the eyes, nose, mouth, vulva and prepuce may be necrotic or ulcerated. The lungs often contain congested, edematous or consolidated areas, and firm gray or white nodules. Nodules have been reported to be particularly common in the diaphragmatic lobes. In the early stages of the disease, they may appear as red spots. Papules or ulcerated papules are common on the abomasal mucosa. Nodules, papules and other lesions may also be found in other parts of the digestive tract, including the rumen, large intestine, pharynx, trachea and esophagus. Pale, discrete subcapsular foci are sometimes present on the surface of the kidney, liver and testes. Lymph nodes throughout the body are usually enlarged and edematous, and they may be congested and hemorrhagic.

Diagnostic Tests

Capripoxviruses, their antigens and nucleic acids can be detected in skin lesions (e.g., biopsies, scrapings, vesicular fluid, scabs); oral, nasal and ocular secretions; blood; lymph node aspirates; and tissue samples from external or internal lesions collected at necropsy. Samples for virus isolation and

for some antigen-detection tests should be collected during the first week of illness, before neutralizing antibodies develop. Blood samples should be taken as early as possible; virus isolation is unlikely to be successful after generalized lesions have been present for more than a few days.

PCR can identify viral RNA directly in tissue samples, blood and secretions. Loop-mediated isothermal amplification tests have also been described in the literature. Most genetic assays can only identify the organism as a capripoxvirus; however, some PCR tests can distinguish the small ruminant capripoxviruses (SPPV and GTPV) from LSDV. Researchers have also described a few specialized PCR-based tests that can specifically identify SPPV or GTPV.

Antigen-detection tests cannot distinguish SPPV, GTPV and LSDV, but they can identify these viruses to the genus level. Tests to detect capripoxvirus antigens include enzyme-linked immunosorbent assays (ELISAs), immunostaining methods and agar gel immunodiffusion (AGID). Cross-reactions with parapoxviruses (e.g., the orf virus) complicate the interpretation of the AGID test; however, these two groups of viruses can be distinguished with electron microscopy. A number of other assays such as counter-immunoelectrophoresis and various agglutination tests have also been described.

SPPV and GTPV can be isolated in various bovine, caprine or ovine cell cultures. They are reported to grow best in lamb testis or small ruminant kidney cell cultures, but other cells can be used. These viruses grow slowly, and may take up to 2 weeks to recover. Isolated viruses can be identified as capripoxviruses by PCR and other genetic techniques, or by antigen-detection methods such as immunofluorescence and virus neutralization. More specific identification is only possibly with certain PCR-based tests.

Histopathology and electron microscopy are also helpful in diagnosis. Electron microscopy can provide a tentative diagnosis, as the morphology of capripoxviruses differs from most poxviruses that cause illnesses in small ruminants.

Serology can identify GTPV and SPPV as capripoxviruses; however, conventional serological tests, including virus neutralization, cannot distinguish GTPV, SPPV and LSDV. A number of serological assays have been described or used, although some of them may not be validated. The World Organization for Animal Health (OIE) Manual of Diagnostic Tests and Vaccines currently describes virus neutralization, the indirect fluorescent antibody test (IFA) and immunoblotting (Western blotting). ELISAs and AGID are also mentioned by some authors, and counter-immunoelectrophoresis was employed in some countries at least as recently as 2010. Cross-reactions can occur between capripoxviruses and other genera of poxviruses in the AGID test and IFA tests. Seroconversion can be poor in some animals, and serology may be most valuable as a herd test.

Treatment

There is no specific treatment for sheep pox or goat pox, but supportive treatment may reduce morbidity and complications.

Control

Disease reporting

Veterinarians who encounter or suspect sheep pox or goat pox should follow their national and/or local guidelines for disease reporting. In the U.S., state or federal veterinary authorities should be informed immediately.

Prevention

Capripoxviruses are most likely to be introduced in infected animals, but they may also enter a herd on fomites and animal products such as wool. Newly introduced animals should be quarantined. Other biosecurity measures, such as prevention of contact with other herds and disinfection of fomites, are also helpful. Infected herds and sick animals should be isolated for at least 45 days after they have recovered from clinical signs. Vaccination is used to control sheep pox and goat pox in endemic areas. Depending on the region, a single vaccine may be employed in all small ruminants, or there may be separate sheep pox and goat pox vaccines.

Outbreaks in non-endemic areas can be controlled with movement controls and depopulation of infected and exposed animals, followed by stringent cleaning and disinfection of farms and equipment. Proper disposal of infected carcasses is important; burning or burial is often used. Insect repellents applied to carcasses might aid in reducing virus transmission before burial, but this has not been evaluated. Waiting periods before restocking can reduce the risk from environments such as pastures, which may be impossible to disinfect. When the disease has spread more widely, vaccination may also be considered.

Morbidity and Mortality

SPPV is generally thought to be more virulent in sheep, and GTPV in goats, although this has not been evaluated for all viruses. Outbreaks often affect only one species, but some sheeppox viruses also cause mild to severe signs in goats, and vice versa. In other cases, asymptomatic infections have occasionally been identified in goats or sheep during outbreaks in the other species. There are also a few reports of incidents caused by the “wrong” virus, such as an outbreak of sheep pox in China that was caused by a virus genetically identified as GTPV.

Morbidity and mortality vary, and may be influenced by the breed of the animal, its age, immunity to capripoxviruses, and the strain of the virus. Mild illnesses are common among indigenous breeds in endemic areas, but more severe disease can be seen in young or stressed animals, individuals with concurrent infections, or animals from areas where pox has not occurred for some time. Reported morbidity rates in indigenous breeds vary widely, ranging from 1% to 70-90%.

Although the overall mortality rate is often less than 10%, it sometimes exceeds 50%, and case fatality rates approaching 100% have been reported in some highly susceptible young animals.

Imported breeds of sheep and goats usually develop severe illnesses when they are moved into an endemic area. The morbidity and mortality rates can approach 100% in some newly imported flocks.

Internet Resources

[European Food Safety Authority \(EFSA\) Scientific Opinion on Sheep and goat pox](#)

[The Merck Veterinary Manual](#)

[United States Animal Health Association. Foreign Animal Diseases](#)

[World Organization for Animal Health \(WOAH\)](#)

[WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals](#)

[WOAH Terrestrial Animal Health Code](#)

Acknowledgements

This factsheet was written by Anna Rovid Spickler, DVM, PhD, Veterinary Specialist from the Center for Food Security and Public Health. The U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) provided funding for this factsheet through a series of cooperative agreements related to the development of resources for initial accreditation training.

The following format can be used to cite this factsheet. Spickler, Anna Rovid. 2017. *Sheep and Goat Pox*. Retrieved from <http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php>.

References

- Aiello SE, Moses MA, editors. The Merck veterinary manual. 11th ed. Kenilworth, NJ: Merck and Co; 2016. Sheeppox and goatpox, p. 869-70.
- Animal Health Australia. The National Animal Health Information System (NAHIS). Sheep pox and goat pox [online]. Available at: <http://www.aahc.com.au/nahis/disease/dislist.asp>.* Accessed 11 Dec 2001.
- Armson B, Fowler VL, Tuppurainen ESM, Howson ELA, Madi M, Sallu R, Kasanga CJ, Pearson C, Wood J, Martin P, Mioulet V, King DP. Detection of capripoxvirus DNA using a field-ready nucleic acid extraction and real-time PCR platform. *Transbound Emerg Dis*. 2017;64(3):994-7.
- Authie E, Berg C, Bøtner A, Browman H, De Koeijer A, Depne K, et al.; EFSA Panel on Animal Health and Welfare Scientific opinion on sheep and goat pox. *EFSA Journal* 2014;12(11):3885.

- Babiuk S, Bowden TR, Boyle DB, Wallace DB, Kitching RP. Capripoxviruses: an emerging worldwide threat to sheep, goats and cattle. *Transbound Emerg Dis*. 2008;55:263-72.
- Babiuk S, Bowden TR, Parkyn G, Dalman B, Hoa DM, Long NT, Vu PP, Bieu DX, Copps J, Boyle DB. Yemen and Vietnam capripoxviruses demonstrate a distinct host preference for goats compared with sheep. *J Gen Virol*. 2009;90:105-114.
- Balinsky CA, Delhon G, Smoliga G, Prarat M, French RA, Geary SJ, Rock DL, Rodriguez LL. Rapid preclinical detection of sheeppox virus by a real-time PCR assay. *J Clin Microbiol*. 2008;46:438-42.
- Barnard BJH. Antibodies against some viruses of domestic animals in South African wild animals. *Onderstepoort J Vet Res*. 1997;64:95-110.
- Ben Chehida F, Ayari-Fakhfakh E, Caufour P, Amdouni J, Nasr J, Messaoudi L, Haj Ammar H, Sghaier S, Bernard C, Ghram A, Cêtre-Sossah C. Sheep pox in Tunisia: Current status and perspectives. *Transbound Emerg Dis*. 2017 Jun 28 [Epub ahead of print].
- Bhanuprakash V, Indrani BK, Hosamani M, Singh RK. The current status of sheep pox disease. *Comp Immunol Microbiol Infect Dis*. 2006;29:27-60.
- Bhanuprakash V, Hosamani M, Singh RK. Prospects of control and eradication of capripox from the Indian subcontinent: a perspective. *Antiviral Res*. 2011;91:225-32.
- Bhanuprakash V, Venkatesan G, Balamurugan V, Hosamani M, Yogisharadhya R, Chauhan RS, Pande A, Mondal B, Singh RK. Pox outbreaks in sheep and goats at Makhdoom (Uttar Pradesh), India: evidence of sheeppox virus infection in goats. *Transbound Emerg Dis*. 2010;57(5):375-82.
- Blackwell JH. Cleaning and disinfection. In: *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association; 1998. p. 445-8.
- Bowden TR, Babiuk SL, Parkyn GR, Copps JS, Boyle DB. Capripoxvirus tissue tropism and shedding: A quantitative study in experimentally infected sheep and goats. *Virology*. 2008;371:380-93.
- Carn VM. Control of capripoxvirus infections. *Vaccine*. 1993;11:1275-9.
- Chu Y, Yan X, Gao P, Zhao P, He Y, Liu J, Lu Z. Molecular detection of a mixed infection of goatpox virus, orf virus, and *Mycoplasma capricolum* subsp. *capripneumoniae* in goats. *J Vet Diagn Invest*. 2011;23:786-9.
- Das A, Babiuk S, McIntosh MT. Development of a loop-mediated isothermal amplification assay for rapid detection of capripoxviruses. *J Clin Microbiol*. 2012;50(5):1613-20.
- Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2004. Sheep pox and goat pox. Available at: <http://www.spc.int/rahs/>.* Accessed 5 Jul 2008.
- Gelaye E, Belay A, Ayelet G, Jenberie S, Yami M, Loitsch A, Tuppurainen E, Grabherr R, Diallo A, Lamien CE. Capripox disease in Ethiopia: genetic differences between field isolates and vaccine strain, and implications for vaccination failure. *Antiviral Res*. 2015;119:28-35.
- Groth A, Gourreau JM, Vassart M, Nguyen-Ba-Vy, Wyers M, Lefevre PC. Capripoxvirus disease in an Arabian oryx (*Oryx leucoryx*) from Saudi Arabia. *Wildl Dis*. 1992;28:295-300.

- Hedger RS, Hamblin C. Neutralising antibodies to lumpy skin disease virus in African wildlife. *Comp Immunol Microbiol Infect Dis*. 1983;6:209-13.
- Hosamani M, Mondal B, Tembhurne PA, Bandyopadhyay SK, Singh RK, Rasool TJ. Differentiation of sheep pox and goat poxviruses by sequence analysis and PCR-RFLP of P32 gene. *Virus Genes*. 2004;29:73-80.
- International Committee on Taxonomy of Viruses [ICTV]. Family Poxviridae; Subfamily: Chordopoxvirinae; Genus Capripoxvirus. *Virus taxonomy: 2016 release EC 48, Budapest, Hungary, August 2016; Email ratification 2017 (MSL #31)*. Available at: <https://talk.ictvonline.org/taxonomy/>. Accessed 18 Jul 2017.
- Kitching P. Capripoxviruses. In: *Foreign animal diseases*. Boca Raton, FL: United States Animal Health Association; 2008. p. 189-96.
- Lamien CE, Lelenta M, Goger W, Silber R, Tuppurainen E, Matijevic M, Luckins AG, Diallo A. Real time PCR method for simultaneous detection, quantitation and differentiation of capripoxviruses. *J Virol Methods*. 2011;171(1):134-40.
- Lamien CE, Le Goff C, Silber R, Wallace DB, Gulyaz V, Tuppurainen E, Madani H, Caufour P, Adam T, Harrak ME, Luckins AG, Albina E, Diallo A. Use of the *Capripoxvirus* homologue of vaccinia virus 30 kD RNA polymerase subunit (RPO30) gene as a novel diagnostic and genotyping target: development of a classical PCR method to differentiate goat poxvirus from sheep poxvirus. *Vet Microbiol*. 2011;149:30-9.
- Le Goff C, Lamien CE, Fakhfakh E, Chadeyras A, Aba-Adulugba E, et al. Capripoxvirus G-protein protein coupled chemokine receptor: A host-range gene suitable for virus animal origin discrimination. *J Gen Virol*. 2009;90:1967-77.
- Mangana O, Kottaridi C, Nomikou K. The epidemiology of sheep pox in Greece from 1987 to 2007. *Rev Sci Tech*. 2008;27(3):899-905.
- Rao TV, Bandyopadhyay SK. A comprehensive review of goat pox and sheep pox and their diagnosis. *Anim Health Res Rev*. 2000;1:127-36.
- Roy P, Purushothaman V, Sreekumar C, Tamizharasan S, Chandramohan A. Sheep pox disease outbreaks in Madras Red and Mechery breeds of indigenous sheep in Tamilnadu, India. *Res Vet Sci*. 2008;85(3):617-21.
- Santhamani R, Venkatesan G, Minhas SK, Shivachandra SB, Muthuchelvan D, Pandey AB, Ramakrishnan MA. Detection and characterization of atypical capripoxviruses among small ruminants in India. *Virus Genes*. 2015;51:33-8.
- Tulman ER, Afonso CL, Lu Z, Zsak L, Sur JH, Sandybaev NT, Kerembekova UZ, Zaitsev VL, Kutish GF, Rock DL. The genomes of sheeppox and goatpox viruses. *J Virol*. 2002;76:6054-61.
- Tuppurainen ESM, Venter EH, Shisler JL, Gari G, Mekonnen GA, Juleff N, Lyons NA, De Clercq K, Upton C, Bowden TR, Babiuk S, Babiuk LA. Capripoxvirus diseases: Current status and opportunities for control. *Transbound Emerg Dis*. 2017;64(3):729-45.
- Venkatesan G, Balamurugan V, Bhanuprakash V. Multiplex PCR for simultaneous detection and differentiation of sheeppox, goatpox and orf viruses from clinical samples of sheep and goats. *J Virol Methods*. 2014 Jan;195:1-8.
- World Organization for Animal Health [OIE]. *Animal diseases data [online]*. Paris: OIE. Sheep pox and goat pox.. Available at: <http://www.oie.int/animal-health-in-the-world/technical-disease-cards/>. Accessed 5 Aug 2017.
- World Organization for Animal Health [OIE]. *Manual of diagnostic tests and vaccines for terrestrial animals [online]*. Paris: OIE; 2008. Sheep pox and goat pox.. Available at: http://www.oie.int/eng/normes/mmanual/2008/pdf/2.07.14_S_POX_G_POX.pdf. Accessed 25 Jul 2008.
- World Organization for Animal Health [OIE]. *Manual of diagnostic tests and vaccines for terrestrial animals [online]*. Paris: OIE; 2017. Sheep pox and goat pox.. Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.07.13_S_POX_G_POX.pdf. Accessed 2 Aug 2017.
- Yan XM, Chu YF, Wu GH, Zhao ZX, Li J, Zhu HX, Zhang Q. An outbreak of sheep pox associated with goat poxvirus in Gansu province of China. *Vet Microbiol*. 2012;156(3-4):425-8.
- Yeruham I, Yadin H, Van Ham M, Bumarov V, Soham A, Perl S. Economic and epidemiological aspects of an outbreak of sheeppox in a dairy sheep flock. *Vet Rec*. 2007;160:236-7.
- Zhao Z, Fan B, Wu G, Yan X, Li Y, Zhou X, Yue H, Dai X, Zhu H, Tian B, Li J, Zhang Q. Development of loop-mediated isothermal amplification assay for specific and rapid detection of differential goat pox virus and sheep pox virus. *BMC Microbiol*. 2014;14:10.
- Zhou T, Jia H, Chen G, He X, Fang Y, Wang X, Guan Q, Zeng S, Cui Q, Jing Z. Phylogenetic analysis of Chinese sheeppox and goatpox virus isolates. *Virol J*. 2012;9:25.
- Zro K, Azelmat S, Bendouro Y, Kuhn JH, El Fahime E, Ennajo MM. PCR-based assay to detect sheeppox virus in ocular, nasal, and rectal swabs from infected Moroccan sheep. *J Virol Methods*. 2014;204:38-43.

*Link defunct