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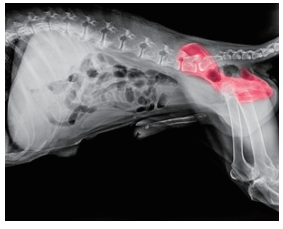
1

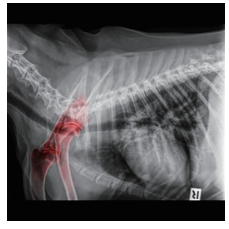
退化性關節炎定義

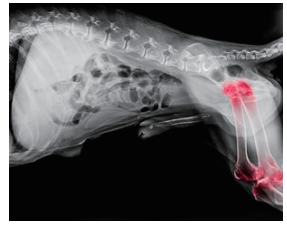
退化性關節炎的定義

美國免疫風濕學會

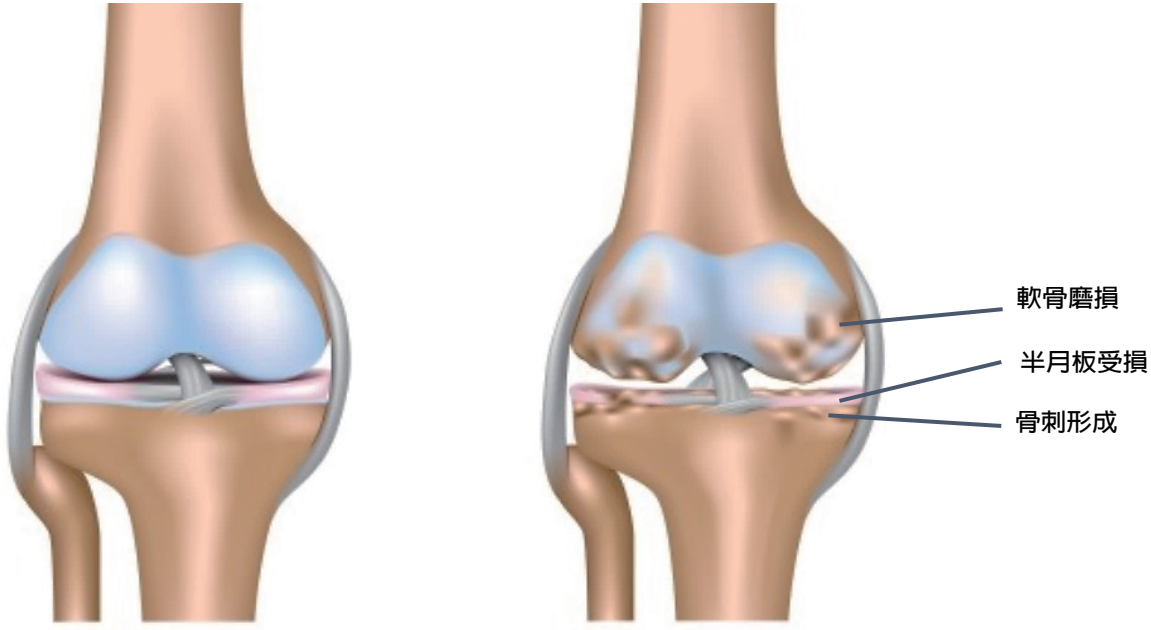
- 不同的成因導致關節的症狀和徵候，主要是關節軟骨有缺陷及結構完整性的破壞以及關節軟骨底部支撐的骨骼結構也惡化。
- 主要的症狀為關節疼痛、僵硬，活動功能喪失。







細部骨骼



Healthy knee joint

Osteoarthritis

Nature Review- Rheumatology 2019 May

Spontaneous dog osteoarthritis — a One Medicine vision

*Richard L. Meeson[1,2,3], Rory J. Todhunter[4,5], Gordon Blunn[3,6], George Nuki[7] and Andrew A. Pitsillides[1]**

Abstract | Osteoarthritis (OA) is a global disease that, despite extensive research, has limited treatment options. Pet dogs share both an environment and lifestyle attributes with their owners, and a growing awareness is developing in the public and among researchers that One Medicine, the mutual co-study of animals and humans, could be beneficial for both humans and dogs. To that end, this Review highlights research opportunities afforded by studying dogs with spontaneous OA, with a view to sharing this active area of veterinary research with new audiences. Similarities and differences between dog and human OA are examined, and the proposition is made that suitably aligned studies of spontaneous OA in dogs and humans, in particular hip and knee OA, could highlight new avenues of discovery. Developing cross-species collaborations will provide a wealth of research material and knowledge that is relevant to human OA and that cannot currently be obtained from rodent models or experimentally induced dog models of OA. Ultimately, this Review aims to raise awareness of spontaneous dog OA and to stimulate discussion regarding its exploration under the One Medicine initiative to improve the health and well-being of both species.

Nature Reviews Rheumatology volume 15, pages273–287 (2019)

2

狗狗退化性關節炎之成因

怎麼判斷犬貓可能有退化性關節炎呢？

狗狗常見狀況如下

- 起身困難
- 如廁困難(不好蹲著大便)
- 活動力下降
- 頻繁舔關節處
- 走路跛行

怎麼判斷犬貓可能有退化性關節炎呢？

貓咪常見狀況如下

- 比較難被主人意識到，但嚴重時會發現到不再跳高處
- 個性行為改變
- 大小便位置改變等
- 走路跛行

退化性關節炎的盛行率

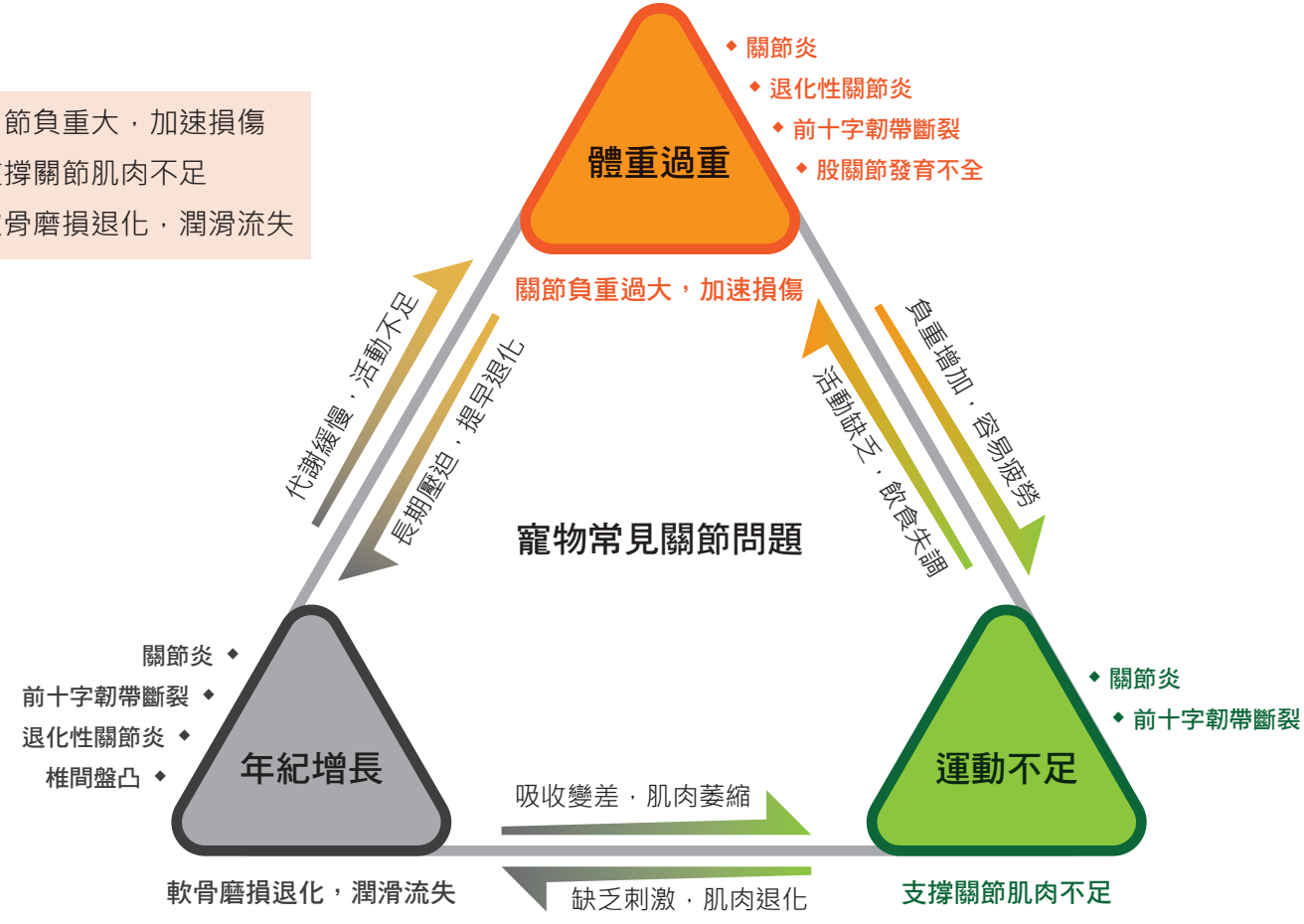
- 在退化性關節炎的盛行率方面，根據美國論文統計，**一歲以上的狗約有20%**有退化性關節炎，**八歲以上則達80%**。英國論文的統計結果也雷同，約有20%的狗狗有退化性關節炎的影像確診。

退化性關節炎的盛行率

- 貓咪的統計上會讓人感到意外！**一歲以上的貓有22%**的比例有退化性關節炎，**十二歲以上的貓咪則是高達 90%**，在影像上可看到退化性關節炎的證據。

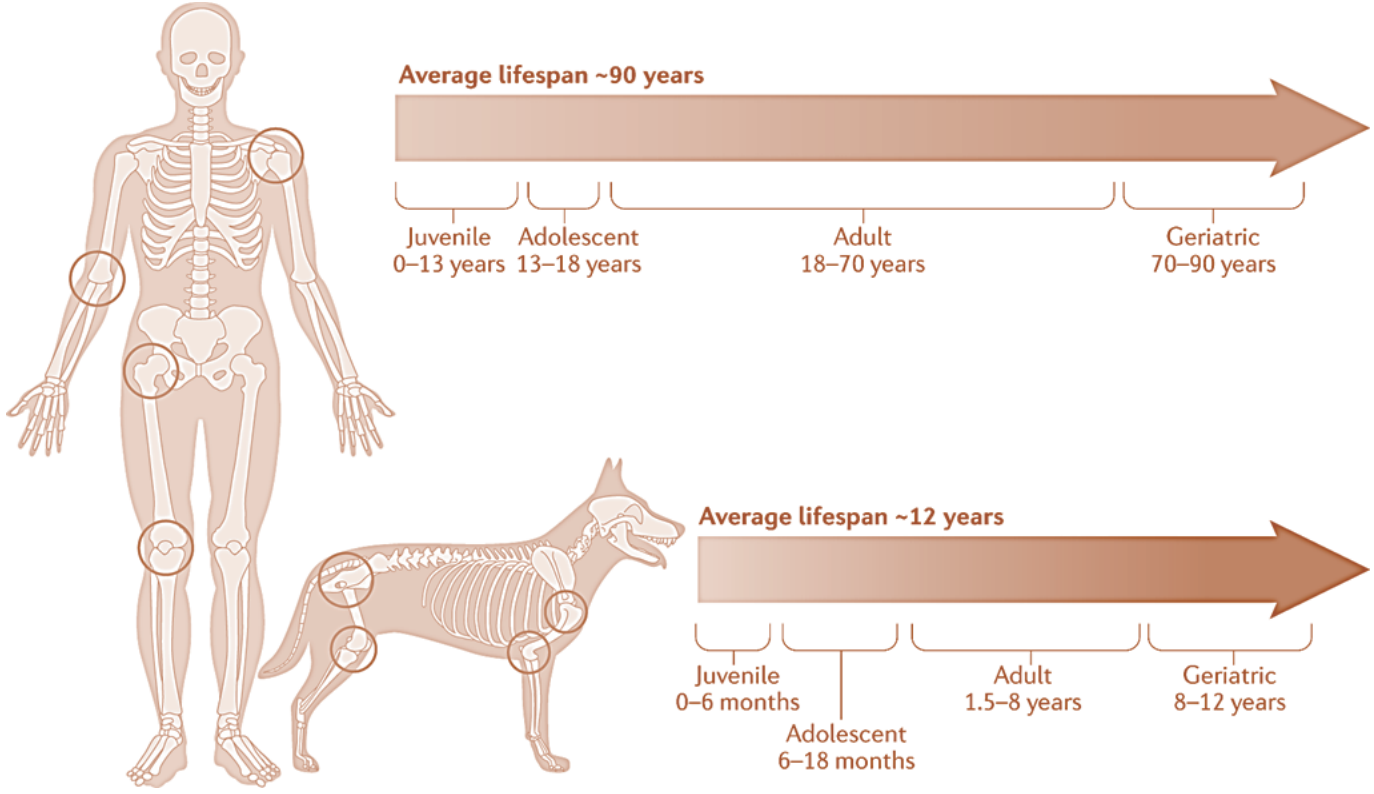
狗狗退化性關節炎之成因

- **體重過重**：關節負重大，加速損傷
- **運動不足**：支撐關節肌肉不足
- **年紀增長**：軟骨磨損退化，潤滑流失



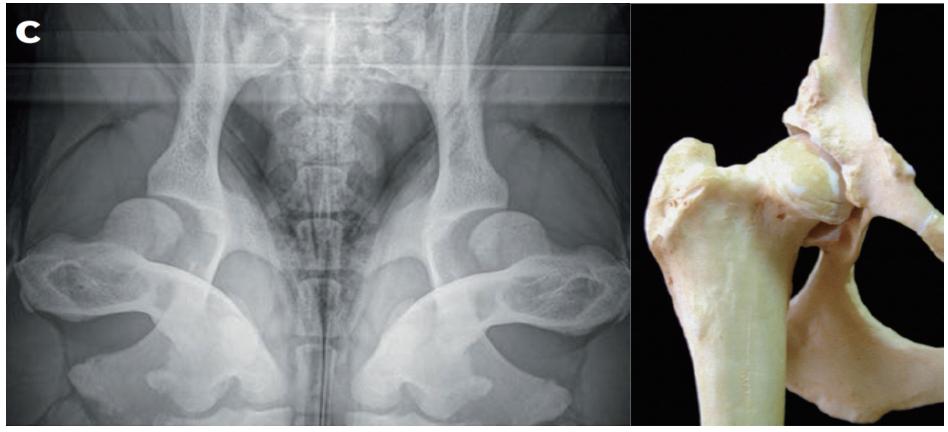
狗骨關節炎最常見的部位

The most common locations for osteoarthritis in dogs include the knee, hip, shoulder and elbow, which are shown with their homologous equivalent in humans.

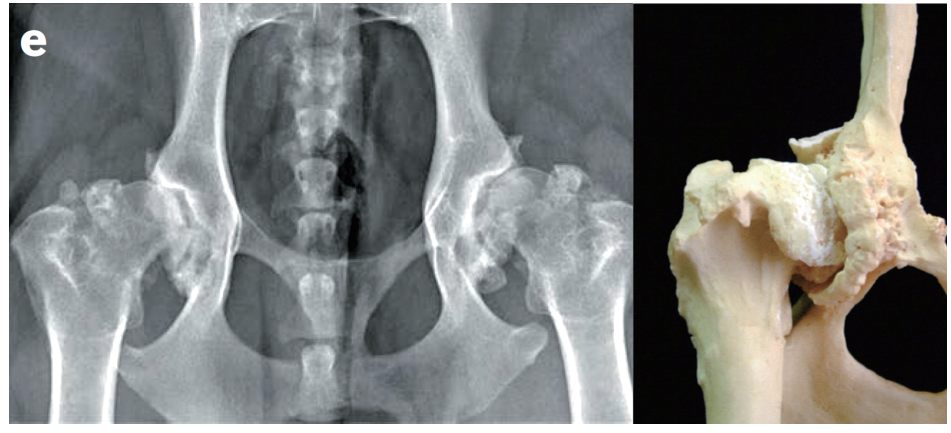


Nature Reviews – Rheumatology 2019;15:273-287.

Healthy dog



Osteoarthritis



退化性關節炎怎麼辦？怎麼治療？

治療目標有三個：

(1)控制疼痛。

(2)增進關節活動及伸展，促進關節囊液的代謝。

(3)幫助修復關節組織。

治療方式又分為：

西醫 (止痛藥、關節保健藥、外科手術、再生醫學)

復健醫學 (雷射、水療、運動復健及居家復健)

中醫 (針灸、中藥、推拿)

3

什麼是鍶(Strontium)?

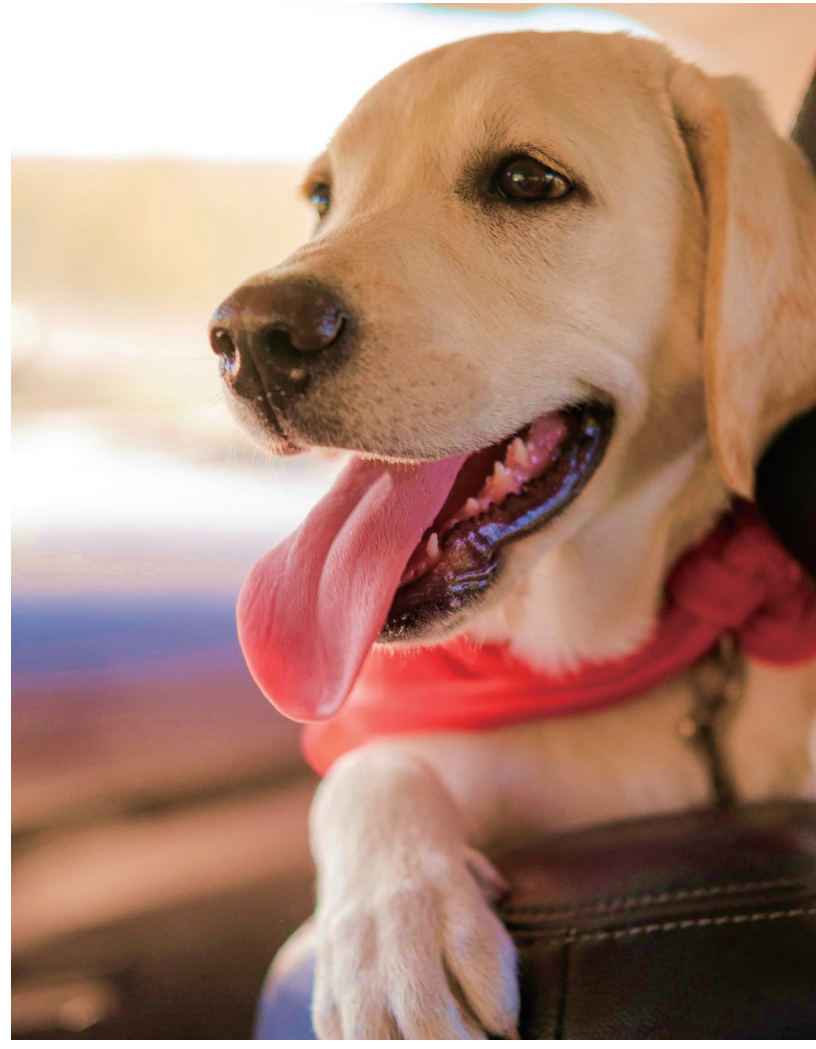
什麼是”鍶”

Strontium

- 1790 年，在蘇格蘭所發現的金屬元素
- 1808 年，由氯化鍶分離出純鍶

  Symbol: Sr　Group: 2A

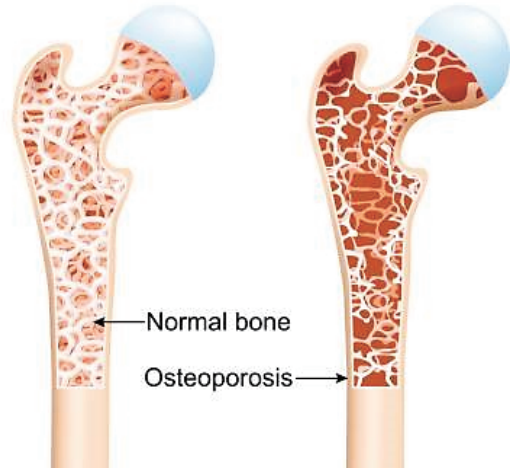
  原子序: 38　原子量: 87.6 approx. (several isotopes exist)
- 1910 年，科學家 Lenherdt 發現“鍶”可以減少骨質流失並同時增加骨質生成
- 1959年，美國梅約醫院對32位骨質疏鬆症患者進行鍶的研究，研究發現每位患者每天服用8克的乳酸鍶，84%的患者表示骨頭疼痛狀況有非常明顯的舒緩，另16%的患者覺得有改善疼痛狀況。
- **1994年，美國FDA食品藥物管理局訂定膳食營養法，將鍶列為食品級原料。**

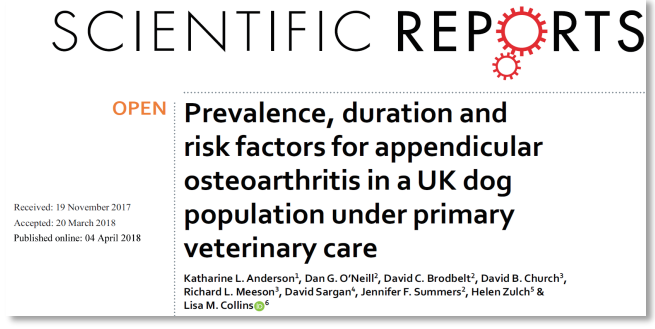


What is osteoarthritis?

何謂骨質疏鬆

- Osteoarthritis is a very common problem in small animals, as it is in humans. It has been estimated that around 30-50% of dogs and cats will be affected by osteoarthritis at some point in their lives. The condition causes long term **degeneration of joints and involves many tissues including cartilage** (the white, shiny, low-friction joint surfaces), **bone under the cartilage, joint capsule and fluid in the joint** (synovial fluid).




SCIENTIFIC REPORTS

OPEN

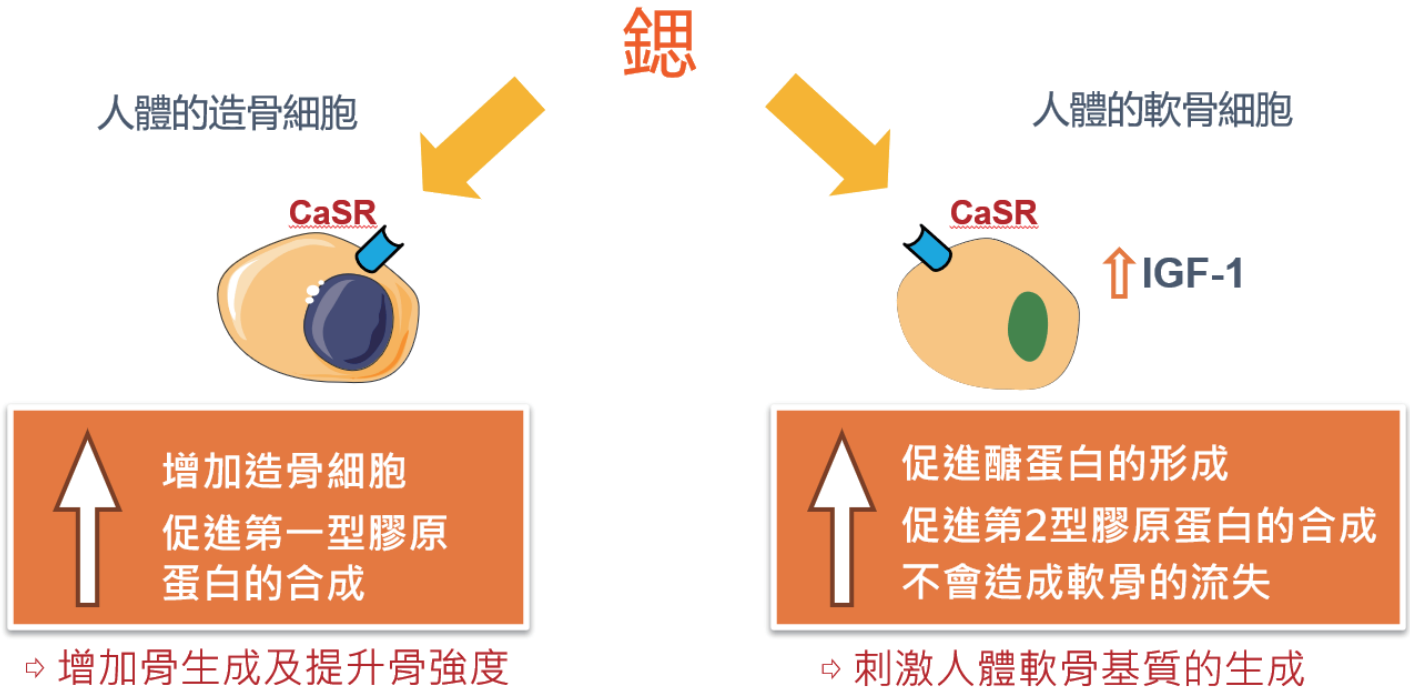
Prevalence, duration and risk factors for appendicular osteoarthritis in a UK dog population under primary veterinary care

Katharine L. Anderson[1], Dan G. O'Neill[2], David C. Brodbelt[2], David B. Church[3], Richard L. Meeson[3], David Sargan[4], Jennifer F. Summers[2], Helen Zulch[5] & Lisa M. Collins[6]

Received: 19 November 2017
Accepted: 20 March 2018
Published online: 04 April 2018

www.nature.com -Scientific Reports 2018

鍶鹽對骨骼的造骨細胞及軟骨之軟骨細胞的作用



Osteoarthritis and Cartilage

International Cartilage Repair Society

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

A review of the effects of insulin-like growth factor and platelet derived growth factor on *in vivo* cartilage healing and repair

M. B. Schmidt Ph.D.†*, E. H. Chen Ph.D.‡ and S. E. Lynch D.M.D., D.M.Sc.§‖

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‖ *Department of Surgery, Vanderbilt University School of Medicine, USA*

Summary

Growth factors may enhance current cartilage repair techniques via multiple mechanisms including recruitment of chondrogenic cells (chemotaxis), stimulation of chondrogenic cell proliferation (mitogenesis) and enhancement of cartilage matrix synthesis. Two growth factors that have been studied in cartilage repair are insulin-like growth factor (IGF) and platelet derived growth factor (PDGF). IGF plays a key role in cartilage homeostasis, balancing proteoglycan synthesis and breakdown. Incorporating IGF into a fibrin clot placed in an equine cartilage defect improved the quality and quantity of repair tissue and reduced synovial inflammation. PDGF is a potent mitogenic and chemotactic factor for all cells of mesenchymal origin, including chondrocytes and mesenchymal stem cells. Resting zone chondrocytes cultured with PDGF demonstrated increased cell proliferation and proteoglycan production, while maturation of these cells along the endochondral pathway was inhibited. Pretreating chondrocytes with PDGF promotes heterotopic cartilage formation in the absence of any mechanical stimulus. PDGF has also been shown to be a potent stimulator of meniscal cell proliferation and migration.

These studies and others suggest a potential role for these potent biological regulators of chondrocytes in cartilage repair. More work needs to be performed to define their appropriate dosing and the optimum delivery method. Combining tissue growth factors with a biological matrix can provide a physical scaffold for cell adhesion and growth as well as a means to control the release of these potent molecules. This could result in biological devices that enhance the predictability and quality of current cartilage repair techniques.

Key words: Insulin-like growth factor, IGF, Platelet derived growth factor, PDGF, Cartilage, Meniscus, Repair.

The effects of Insulin-like growth factor on cartilage healing and repair

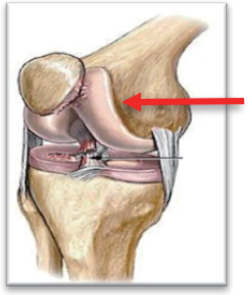
Strontium salt–Rationale in OA
In vivo results

A 16-week osteoarthritis intervention study in the dog ACL model

4 weeks | **12 weeks**

Treatment initiation

Mean weight: 25 ± 3 kg



Anterior Cruciate Ligament section (right knee)

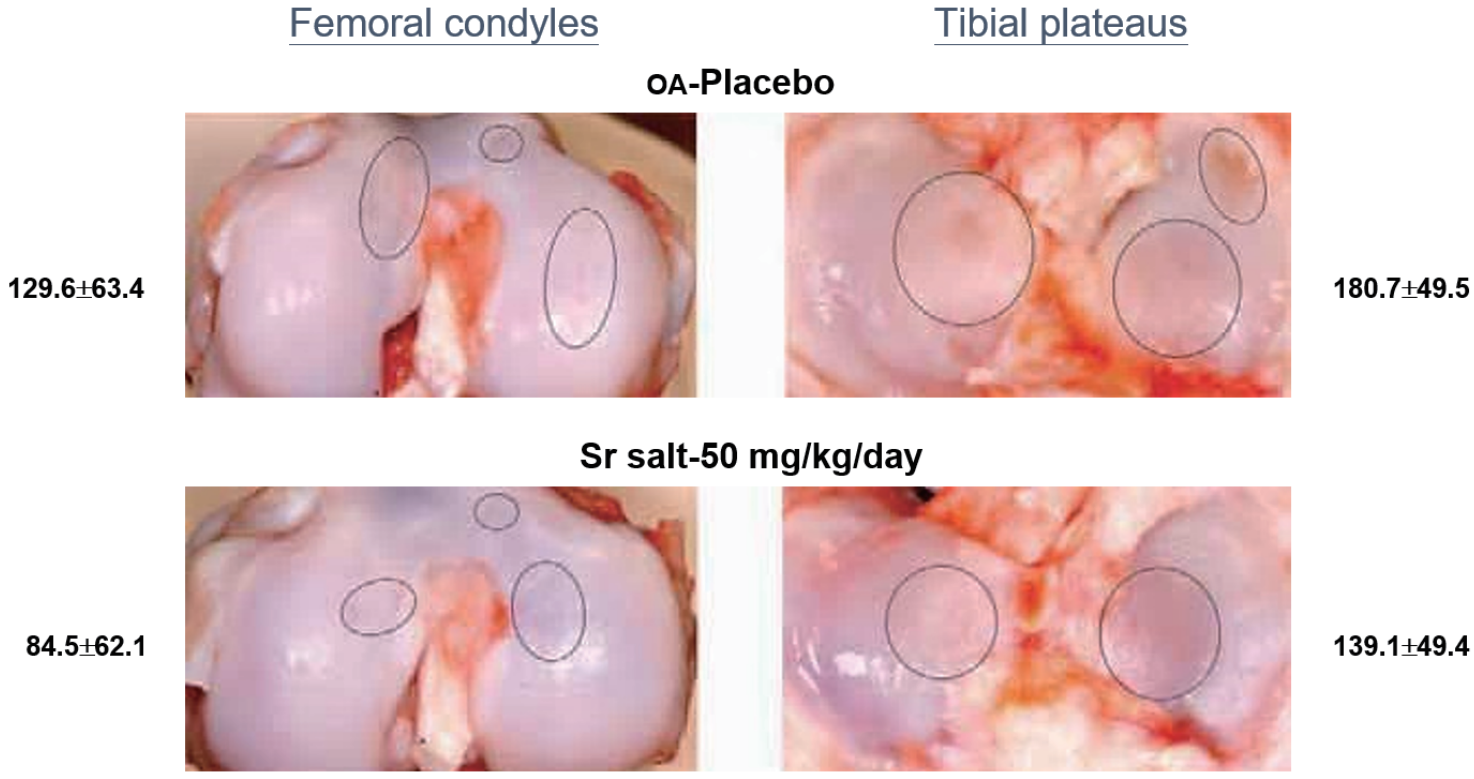
N=40 dogs: 25, 50, 75 mg/kg/day of Sr salt orally *versus* placebo.

The morphological observers blinded to the treatment groups.

- **To investigate:**
  - Macroscopic lesions of cartilage between femoral condyles and tibial plateaus.
  - Changes of subchondral bone plate
  - **Cartilage & synovial key proteases**
    - ➢ IL-1β, MMP-1, MMP-13, ADAMTS5, cathepsin K

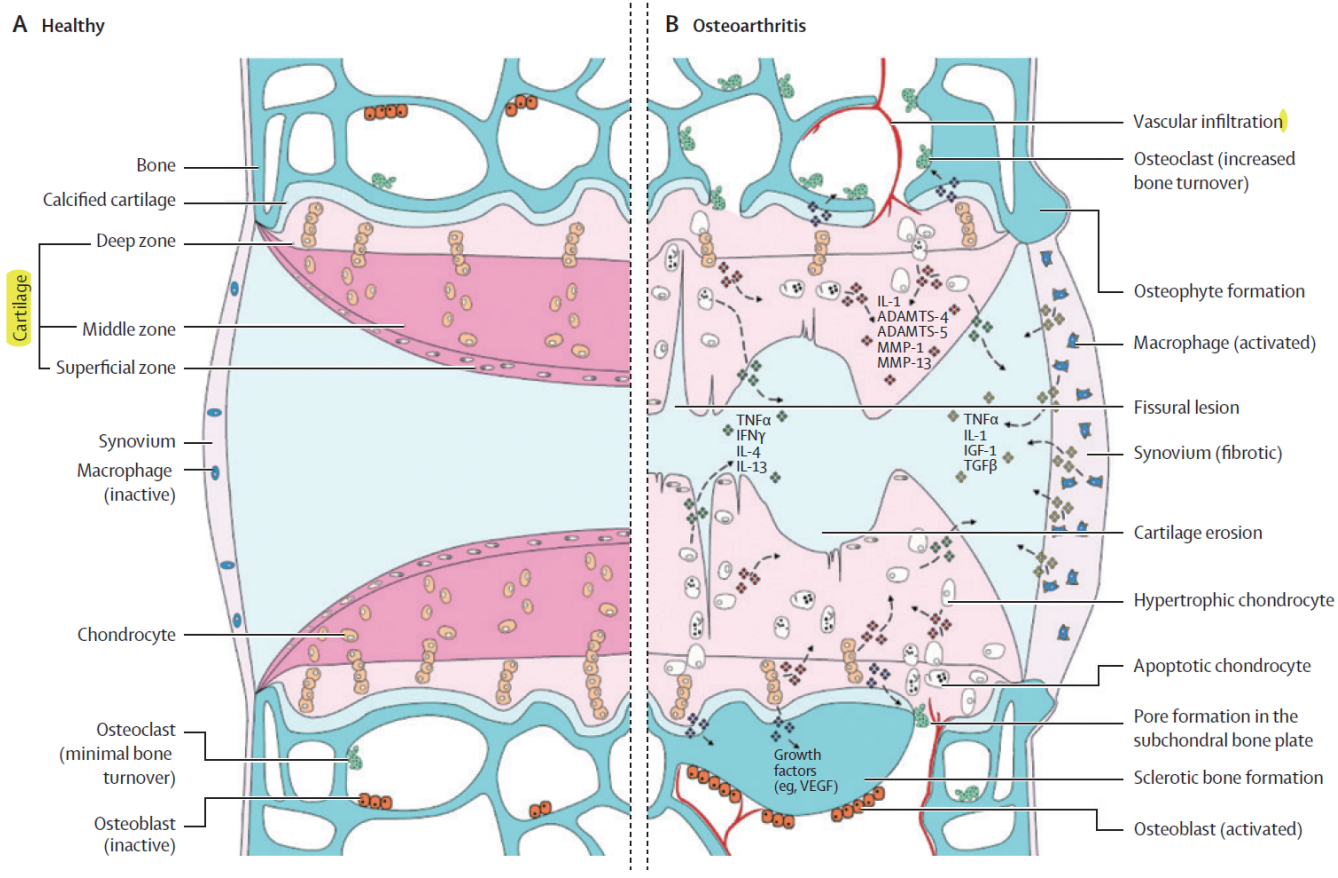
JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

Macroscopic appearance of cartilage (16 weeks)



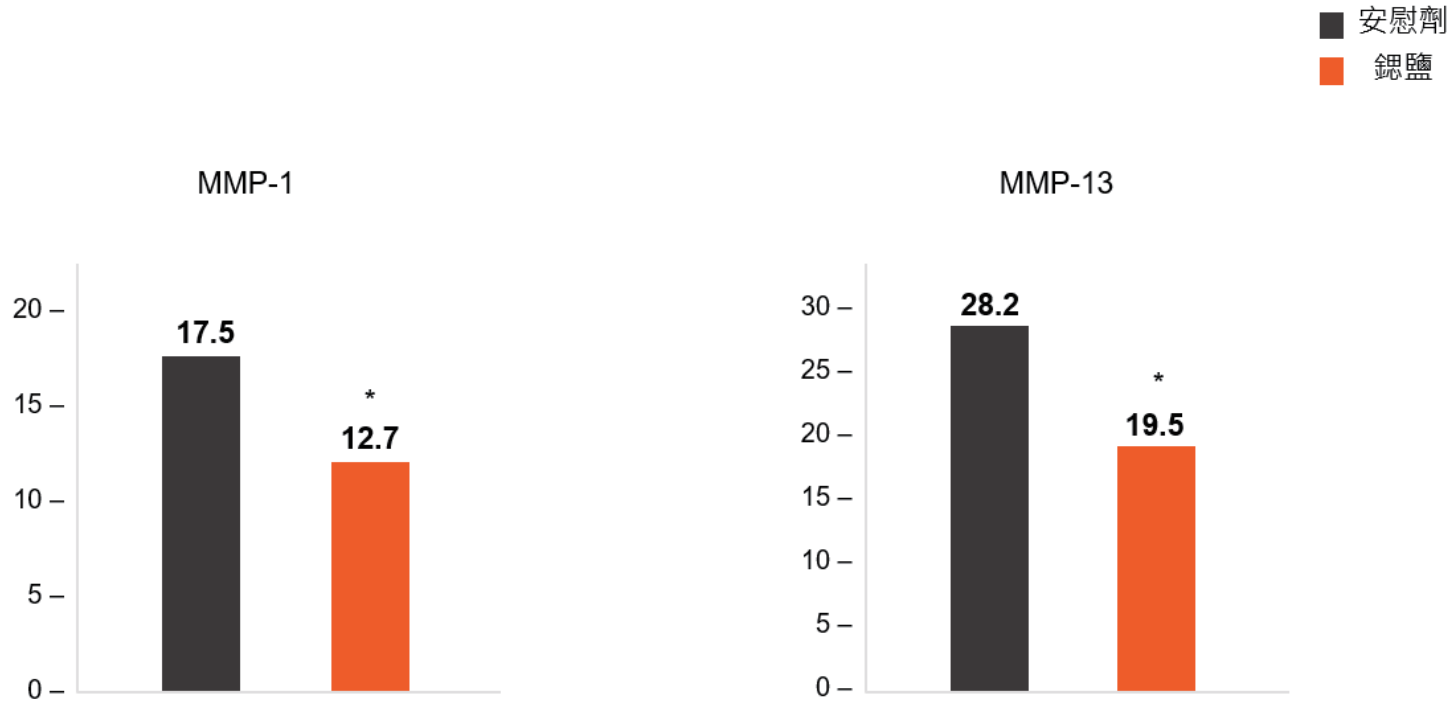
JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

造成退化性關節炎的機轉



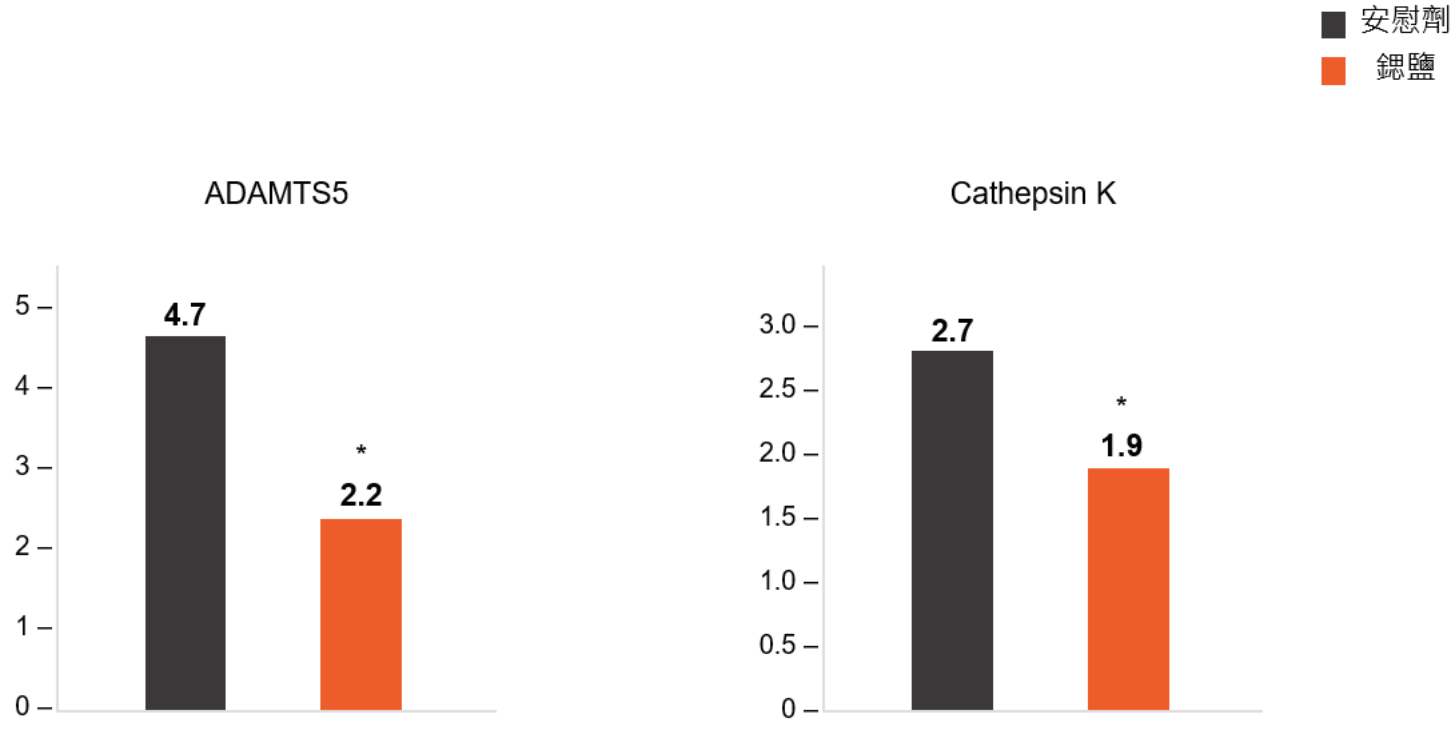
S Glyn-Johns, AJR Paimer et al. Lancet. 2015 March.

鏁鹽明顯降低關節軟骨之分解酶



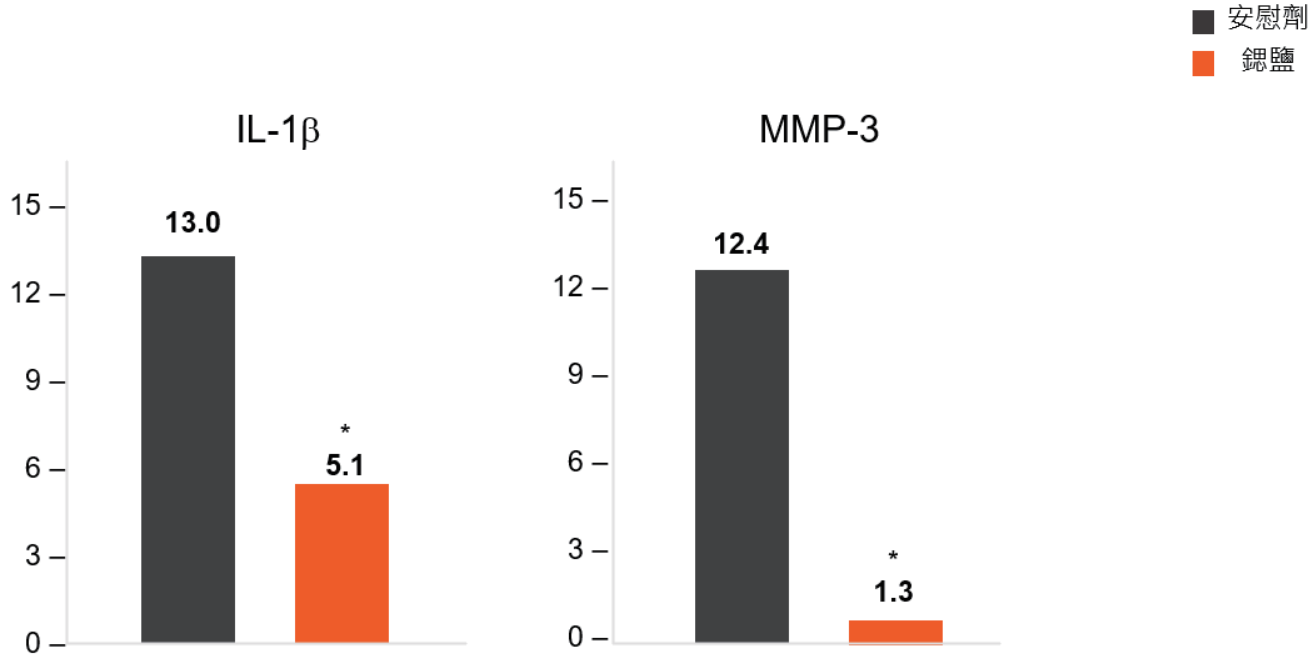
JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

鏗鹽明顯降低關節軟骨之分解酶



JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

鏗鹽明顯降低關節滑液膜之發炎指標



Safety

All dogs completed the study and the treatment was well tolerated throughout the dosing period. There was no significant change in the weight of the dogs or evidence of any meaningful side effects during the conduct of the study.

JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

CANINE MOBILITY

Investigation and management of canine osteoarthritis

Rob A. Pettitt, Alexander J. German

Lameness in dogs will be a familiar part of any small animal practitioner's caseload. Osteoarthritis is a common cause for this lameness, although it is often secondary to a primary inciting cause; so treatment and management may need to address the primary inciting cause as well as the pain associated with the arthritis. Management of the condition involves a combination of medical and surgical options, and weight management can often be crucial in reducing pain and improving patient mobility. In this article, Rob Pettitt and Alex German explore the multifactorial elements in both investigating and managing this condition in dogs.

In vitro work into glucosamine has shown that it can alter chondrocyte metabolism and this is the rationale for its use in osteoarthritis. However, the efficacy of glucosamine in vivo remains unproven and evidence is lacking as to whether oral glucosamine reaches the chondrocytes in any useful form. Similar findings have been seen with chondroitin sulphate where there has been much debate over whether the molecule reaches articular cartilage intact or as a depolymerised version. The benefits of nutraceuticals in the management of osteoarthritis are debatable and two large double-blinded negative-controlled studies reported no significant efficacy (Moreau and others 2003, Clegg and others 2006) and current evidence remains insufficient to endorse their efficacy in the management of canine osteoarthritis.

R.A. Pettitt et al. In Practice FOCUS. November 2015.

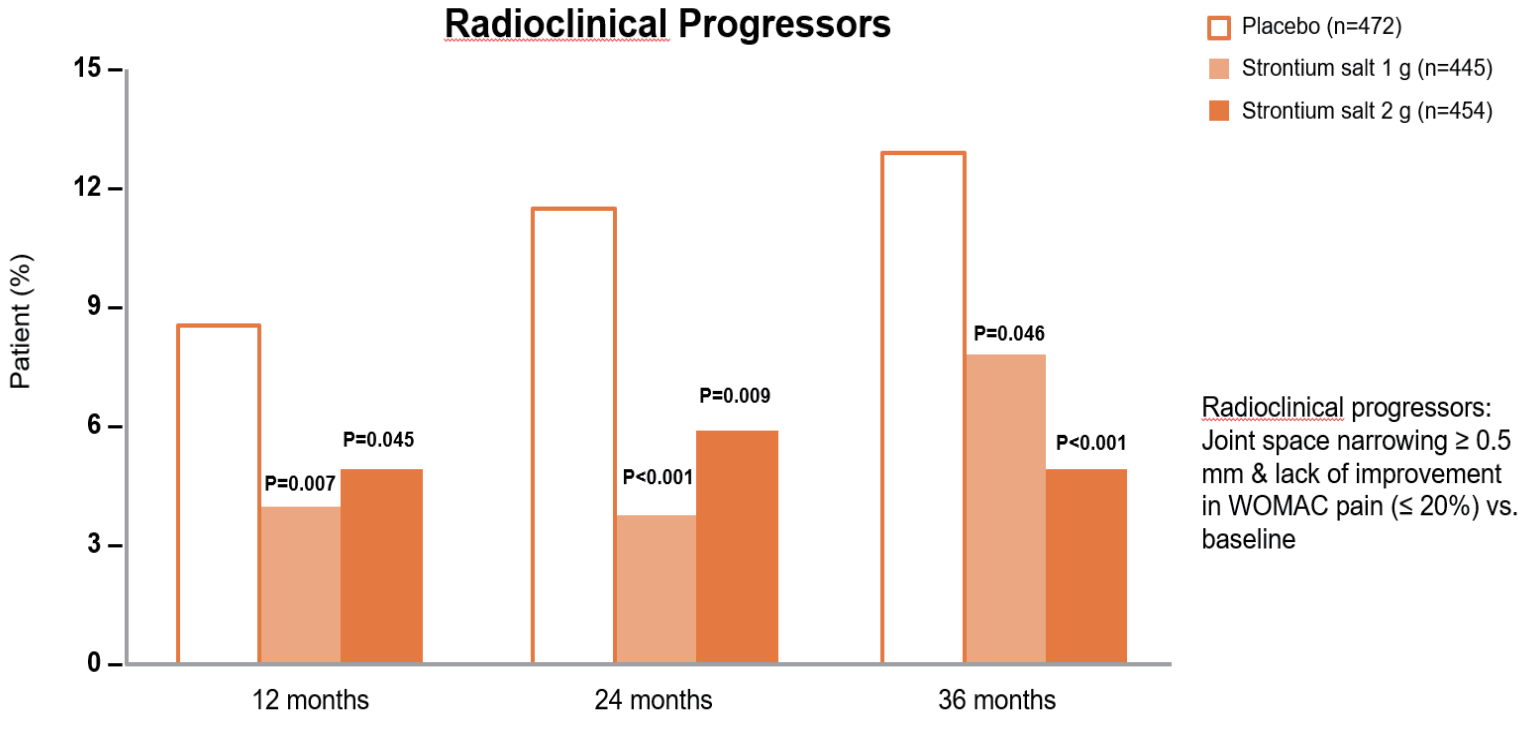
LANCET – March 4, 2015
Osteoarthritis

Glucosamine and chondroitin;[106] hyaluronic acid[107]	Meta-analyses do not show improvement in symptoms or structure over placebo
Doxycycline[108]	Structural modification but no symptomatic benefit
FGF-18 (intra-articular)[109]	Structural modification but no symptomatic benefit
Pharmaceutical: targeting bone remodelling	
Strontium ranelate[110]	Improvement in symptoms and structure

	Outcome	Comments
Lifestyle modification		
Weight loss;[95-98] exercise[99] (strength and aerobic capacity)	Symptom improvement and reduced risk of symptomatic osteoarthritis MRI and biochemical marker evidence of structural modification	Potential role as primary prevention strategy
Surgical modification of joint biomechanics		
Periarticular osteotomy[100,101] (to correct mechanical axis of knee or orientation of acetabulum)	Established technique for improvement of symptoms and probably joint survival	Suggested potential for cartilage regeneration after these procedures
Debridement of FAI lesions[102]	Symptom improvement sustained beyond 5 years	Small cohort studies only; structural modification not yet shown; RCTs underway
Joint distraction[103] (6–12 weeks)	Sustained symptomatic improvement with evidence of cartilage regeneration	Best evidence so far that cartilage can regenerate in an osteoarthritic joint
Regenerative surgical techniques		
Microfracture of subchondral bone[104]	Slight improvement in pain and defect filling	Produces mechanically inferior fibrocartilage rather than hyaline cartilage
Cell-based therapies[104,105] (autologous chondrocyte implantation)	Slight improvement in pain and defect filling	Might provide more durable repair tissue than microfracture but further studies are needed; technique is expensive
Pharmaceutical: targeting cartilage degradation		
Glucosamine and chondroitin;[106] hyaluronic acid[107]	Meta-analyses do not show improvement in symptoms or structure over placebo	Conflicting results from different studies
Doxycycline[108]	Structural modification but no symptomatic benefit	Limited by side-effects
FGF-18 (intra-articular)[109]	Structural modification but no symptomatic benefit	Primary outcome measure of structural change in medial compartment not shown
Pharmaceutical: targeting bone remodelling		
Strontium ranelate[110]	Improvement in symptoms and structure	Limited by side-effects

JP Pelletier et al. Ann Rheum Dis. 2013 Feb;72(2):250-257.

鍶鹽在人類退化性關節炎的療效



Radioclinical progressors: Joint space narrowing ≥ 0.5 mm & lack of improvement in WOMAC pain (≤ 20%) vs. baseline

JY Reginster, C Cooper, et al. Ann Rheum Dis.. 2013 Feb;72(2):179-86

Beynen AC, 2021. Strontium in petfood

Article · March 2021

water and soil, thus also entering plants and livestock. Strontium is not intentionally added to petfood. Regular ingredients bring along the element as an intrinsic component. Analysed contents of strontium in kibbled and canned petfoods varied from 5 to 190 mg per kg dry matter (or per kg of the food's residue after removal of its moisture).

There are no indications that strontium is an essential nutrient for dogs and cats. Research data indicate that part of the strontium ingested by dogs and cats crosses the intestine and is subsequently excreted in urine. Circumstantial evidence indicates that strontium in petfood is safe for dogs, including in the long term. Seemingly, the same holds for cats, but the designations are weak.

Plasma strontium

It has been proposed that oral strontium is useful in the treatment of osteoarthritis (Note 13). Based on indicators, it has been concluded (13) that ingested strontium ranelate ($C_{12}H_6N_2O_8SSr$) reduces the progression of surgically-induced osteoarthritis in dogs. The dogs (n=10/group) received

Requirement

In the light of the osteoarthritis study (13), strontium might have pharmacological potency in dogs.

Toxicity

In 2005, the Committee on Minerals and Toxic Substances in Diets and Water for Animals (18) concluded: "strontium is not a toxicological concern for animals". That conclusion is based on data indicating that cattle, swine and chickens can tolerate strontium amounts that are 100 to 1,000 times greater than those normally found in their diets. Early single strontium challenges via various routes also revealed low toxicity in dogs (Notes 18-20) and cats (Note 21).

結論 Conclusion

- **退化性關節炎不只是關節軟骨的流失及退化**，關節軟骨底部支撐的骨骼結構也惡化。
- 鍶鹽的作用機轉不但能促進骨生成，亦可增加軟骨組織的生長。
- 國際知名醫學期刊證實**鍶鹽對中大型犬能有效治療退化性關節炎，對人類的退化性關節炎亦有明顯的療效**。
- **人類營養學暨動物營養學的教授**Anton Beynen**在最新**Strontium in petfood, March 2021) **的專論中證實，縱然在高劑量下鍶對動物是沒有毒性的。**

Biography of Anton C. Beynen

Anton C. Beynen was born in 1953. As from 1987 he has held 7 different professorships. He now is head of Research and Development for Vobra Special Petfoods BV, Veghel. The Netherlands.

Anton Beynen has a M.Sc. of human nutrition (1977) and wrote a Ph.D. thesis (1981) on the regulation of fat metabolism. As a professor at Wageningen University, The Netherlands (1987-1992), at the University of Indonesia, Jakarta, Indonesia (1991-1993), at Utrecht University, The Netherlands (1993-1998, 1995-1999, 1999-2007), at Rajamangala University of Technology-Isan, Sakon Nakhon (2006-now) and at King Saud University, Riyad, Saudi Arabia (2009-2014) he has supervised PhD students and taught basic and applied animal nutrition to students of veterinary and biomedical sciences. Anton Beynen carries out research, the main topic now being diet in health and disease in dogs and cats.

In 1993 Anton Beynen received, as the first non-US investigator, the Bio-Serv Award of experimental animal nutrition. In 2000 he was honoured as best teacher of the Faculty of Veterinary Medicine and in 2002 he was the most prolific supervisor of Ph.D. students of Utrecht University. Anton C. Beynen has served on the editorial board of 12 international journals, is supervisor of 51 completed Ph.D. theses and is (co)author of more than 700 publications of which 430 are indexed by PubMed (www.ncbi.nlm.nih.gov) and has been recognized as highly cited author in the area of agricultural sciences (www.isihighlycited.com).

Thank you

Please contact us for more info.

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