Pan European Networks

LiesegangTeam

Bone to bone marker

Falling for bone and cartilage metabolism – Professor Dr Annette Liesegang discusses the possibilities of measurements in animals and animal models

There is a strong relationship between formation and resorption of bone as well as in cartilage in humans and in animals. Bone turnover and cartilage turnover can be monitored non-invasively by using biochemical bone markers or cartilage markers, which are enzymes and other protein products released by osteoblasts/chondroblasts and osteoclasts/chrondroclasts respectively.

Biochemical markers

The biochemical markers of bone formation currently in use include bone isoenzyme of alkaline phosphatase, osteocalcin and propeptides derived from terminal ends of the type I procollagen molecule. The most useful markers of bone resorption are breakdown products of type I collagen. The longest established method is the measurement of hydroxyproline (HYP) in urine, which is not specific for bone, because it can be found in all collagen types and is also derived from the diet. The measurement of collagen crosslinks, deoxypyridinoline (DPD) and pyridinoline (PYD) is comparatively more specific to monitor bone resorption. DPD and PYD are of use in human medicine in the diagnosis and evaluation of bone diseases and in the prediction of the occurrence of fractures and the rates of bone loss. The carboxyterminal telopeptide of type I collagen (ICTP), which has been used in several animal species, is also a promising bone marker.

There are other degradation products of type I collagen of the organic bone matrix such as serum CrossLaps (CTX), which is a marker of bone resorption. Biochemical markers for cartilage degradation (CTX-II, C2C, C1,2C and COMP) and cartilage synthesis (CPII, CS846 and YKL-40) have also been used in many studies.

Growth diagnosis

These may be new possibilities for diagnosis of growth retardment or growth disorders (extent of joint destruction), prediction of disease progression (in humans) and rapid assessment of the efficacy of therapy (humans). For both tissues, the ratio of bone (or cartilage) resorption markers and formation markers is used to objectify the remodelling of these tissues. These markers have been extensively investigated by the team at the Institute of Animal Nutrition, where the courses of different bone markers in different species, especially during gestation and lactation, were studied in comparison to human medicine. Various influences on the interactions between bone resorption and formation were also studied there.

The basic research of Professor Dr Annette Liesegang was focused on the importance of physiological and nutritional influences on bone resorption and formation. The institute is expert in many species (ruminant, dog, reptile, pig, chicken), especially those to be used as models for human medicine. Recently, the work is also focused on calcium absorption in the intestines, where immunohistochemical methods as well as western blot have been developed. In this area until now, several research projects were and are published. The same is true for the action of Vitamin D under UVB radiation or as supplement in nutrition.

Diagnostic imaging

Another possibility to monitor bone metabolism is the use of diagnostic imaging in humans and animals. Bone strength has been shown to depend on the amount and density of bone present. On the basis of this relationship, several techniques have been developed to measure the bone mineral density (BMD) and the bone mineral content (BMC) non-invasively at different skeletal sites.

Peripheral quantitative computed tomography (pQCT) has become an established method for evaluating the skeletal status, assessing osteoporosis, determining fracture risk and monitoring metabolic diseases and therapies in humans.

In veterinary medicine, the application of pQCT technology is still rare, although this methodology has the potential to be an important research and clinical tool for, for example, the study of endocrine and metabolic diseases that affect the calcium-phosphorus balance, orthopaedic diseases and fracture risks.

At the Institute of Animal Nutrition, the Liesegang team is mainly dealing with problems related to bone and cartilage physiology and the impact of nutrition in this field. Many studies have been realised where the focus was put on bone metabolism in the context of osteoporosis. Mainly sheep and goats were used as animal models, but pigs are also of high interest in this context as well as rats or mice. The Institute of Animal Nutrition also has facilities and infrastructure to conduct animal experiments. Animal stables are available as well as a laboratory. Animals will be taken from the institute's own sheep and goat herd, which are managed with veterinary care.

Future avenues

It is important to study the regulatory mechanism on a systemic as well as on a cellular level. Furthermore, elucidating the systemic effects and controlling the development of bone mineral content and density, plus the course of selected bone markers, are opening up future avenues to treating patients more effectively through therapeutic interventions based on modern approaches with biotechnology.

Parathyroid hormone (PTH) secreted from the parathyroidea plays an important role on mineral metabolism and bone remodelling. Under physiological circumstances, 1.25$(OH)_2$-Vitamin D plays a minor role in the influence on bone but increases the absorption of calcium and phosphorus, which are essential for the mineralisation of bone. Other important hormones are the growth hormone and the insulin-like growth factors (IGFs), which influence the epiphyses and are the predominant factors for a normal skeletal development. All these hormones are intensively studied under different special focuses at the Institute of Animal Nutrition.

A number of studies have described the measurement of biochemical markers of bone cell activity in humans, sheep, horses, pigs, cattle, dogs, chickens and birds and have shown dynamic changes in bone cell function associated with skeletal maturation, exercise, ovariectomy, osteomyelitis and the effects of hormones and drugs on the skeleton. In general, the measurement of markers of bone cell activity remains exclusively a method used in scientific research in animals, although there is an increasing amount of work being undertaken worldwide on their potential clinical applications in companion animals, particularly in dogs and horses.

Within the surrounding CABMM, many possibilities are given since the Institute of Animal Nutrition is able to use the whole infrastructure as well as parts within this infrastructure and deliver their expertise and laboratory skills to the other partners. These sophisticated tools are available to all institutions which need this expertise within their projects and with this give their work and ours more impact.

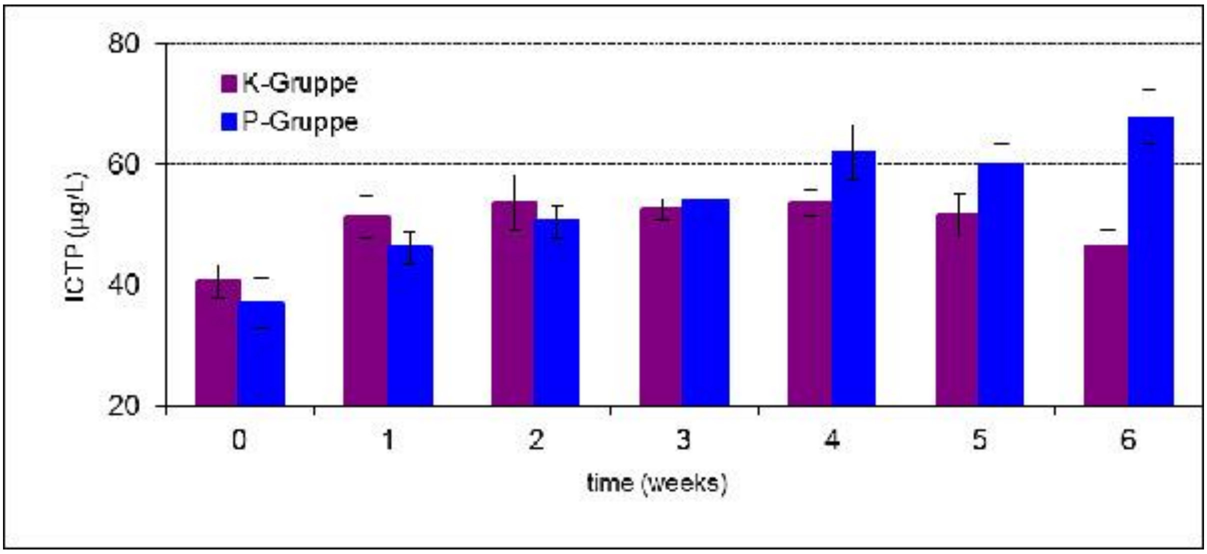

Fig. 1 Bone resorption marker (ICTP) in two different groups of pigs over six weeks. The time pattern shows a diet-induced bone resorption. * = significant differences

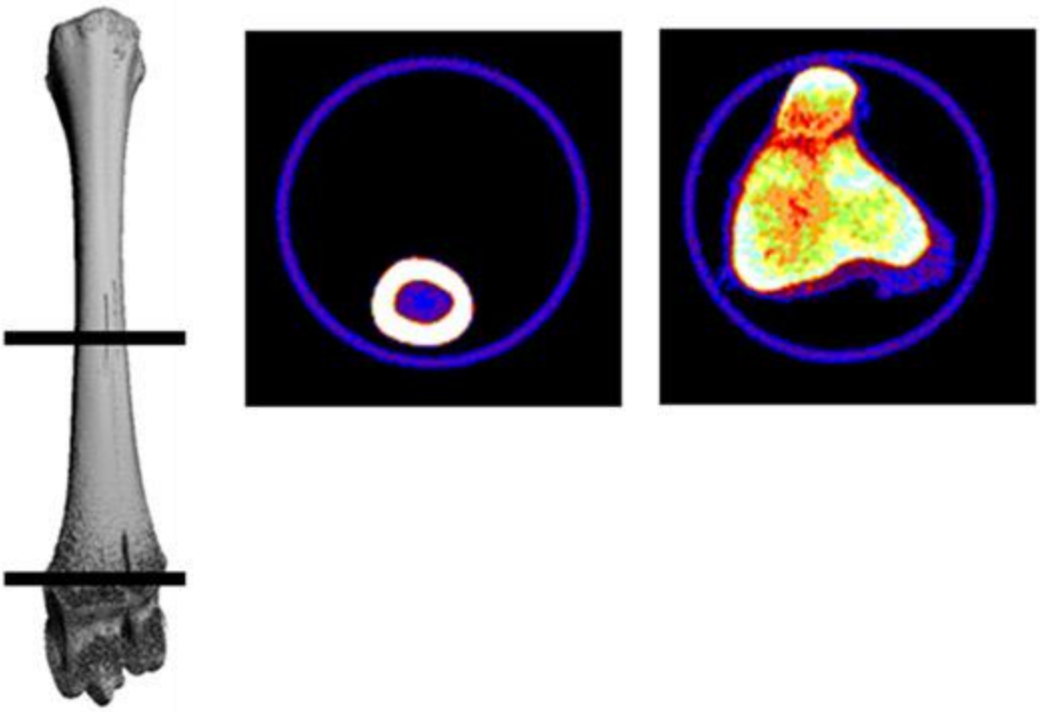

Fig. 2 Peripheral quantitative computer tomography – to measure bone mineral density and content in living animals over a longer period of time. A – Diaphysis, B – Metaphysis, White = mineralised bone

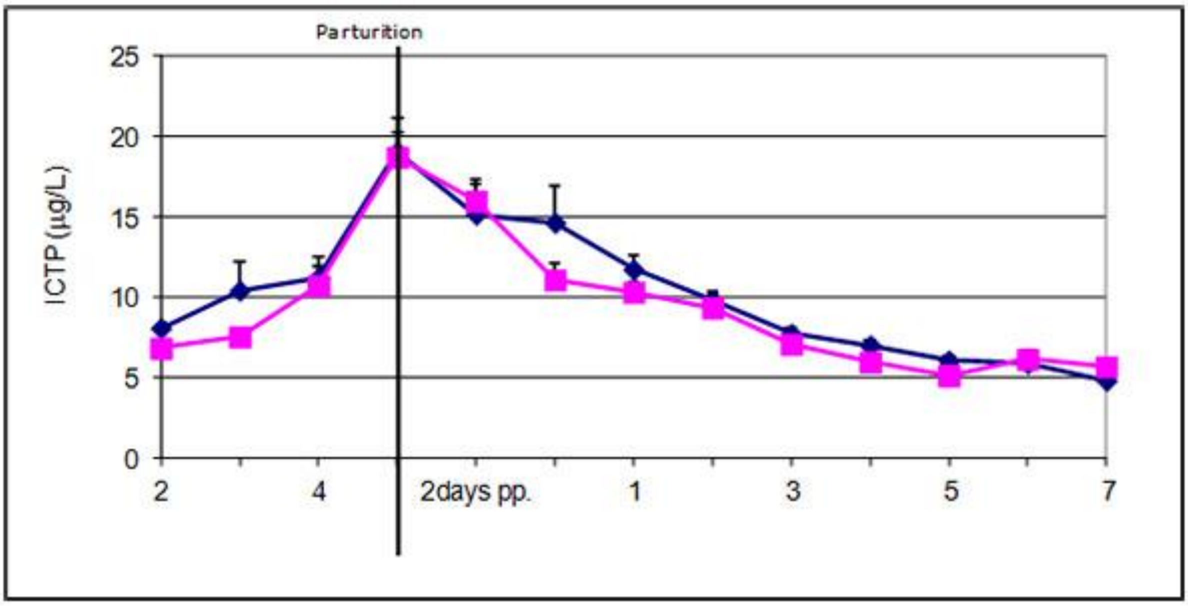

Fig. 3 Bone density as well as cortical thickness (white ring very thin, blue surrounding is muscle) decrease, while bone resorption increases at the beginning of lactation in small ruminants. Already some days after parturition, the bone seems to 'recover' and bone density as well as the cortical thickness increase again (white cortical bone is thicker again). Pink = goats' milk, blue = sheep's milk

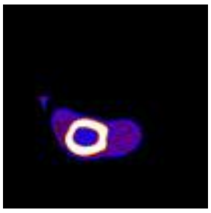

Fig3a

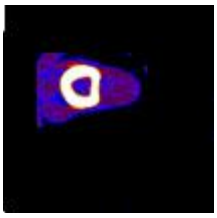

Fig3b

Prof Dr Brigitte von Rechenberg
Chair
Competence Centre for Applied Biology & Molecular Medicine
tel: +41 446 358 410
bvonrechenberg@vetclinics.uzh.ch
http://www.cabmm.uzh.ch/index.html