伴侶動物の肥満と健康障害

Obesity in Companion Animals

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The title of my talk is about obesity and health issues in companion animals. As the main topic of this conference is about the rescue of animals, maybe it does not seem to relate to obesity but we have been hearing about GI related issues. So now we will move to the topic of obesity, and from the viewpoint of nutrition, I will address the current situation for companion animals. I would like to discuss the issues and share some study data and about how obesity is related to disease as well.

In relation to human beings the phrase "metabolic syndrome" is now very commonly used. The words are common and the phenomena itself is expanding. But how about cats and dogs? Do they have metabolic syndrome? That is what I wish to discuss.

I will show you some information relating to people, albeit very rough data about the World Population. It shows that about half of all people have some kind of abnormality as identified by nutrition experts. Half of the numbers relate to dystrophy due to malnutrition in developing countries. The rest refer to obesity in the advanced countries, something which is very special and a quite unique situation, occurring for the first time in the long history of mankind. But it has become not only a human issue and nowadays we have begun to see obesity in cats as well. This obesity in companion animals has been coming to prominence during the past twenty years. Of course it does differ due to geographic differences but we see it in mainly urban areas of advanced countries especially. It is now being said that 30% of dogs and cats in such areas are obese. This is data for the United States, the UK, Australia as well as in Japan.

But why is it that we say obesity is so bad? In human beings we are discussing it as 'metabolic syndrome'. But what exactly is it? Well, the definition is quite difficult. Obesity refers to visceral fat in which the fat accumulates in visceral cavity, and as a result, leads to hypoglycemia, hyperlipidemia and hypertension which inhibit blood flow. If such diseases are detected it can be summarized as metabolic syndrome which will lead to early diabetes and arteriosclerosis. Suffering from diabetes has an impact on the cardiovascular system.

Later I will touch upon how metabolic syndrome relates to dogs and cats but before I do that I wish to talk about the basis of obesity. The basis is obviously too much body fat with the fat being accumulated excessively but we need to ask about the cause of obesity. Sometimes there are specific diseases involved, but it is about comparing the difference between original intake or consumption and energy used. If the difference is too much, obesity arises. So it is usually said that eating too much and exercising too little is the real cause. But the matter is not as simple as that. Modern day genetic studies have concluded that there are more difficult and complicated factors involved in the background. So I would also like to touch upon this research in my talk.

Just before I go into that I should say that when we think about obesity we should never forget that our entire humankind history, like that of animals, has been one of suffering through a long battle to fight starvation. If we were to express our own history as one 24 hour period then we can say that for 23 hours, 59 minutes and 9 seconds we were starving. It has only been for 51 seconds that we have been satisfied. So suffering from obesity is a quite recent issue and until recently we have been fighting starvation. Our body structure has changed throughout evolution to reflect that struggle. The features not needed for that battle were discarded during the process of evolution. But those we did need for the battle were retained in our genes and refined further.

And so from the viewpoint of such historical analysis, obesity is a recent history phenomenon. Something abnormal has begun to occur. Considering our time span as exceeding billions of hours, obesity has had such a miniscule period of existence that we don't have much knowledge about it yet. My slide shows some of the research, which is at quite an academic level. But let me talk about leptin. This was only discovered just over 10 years ago and the data I am showing is from the UK magazine 'Nature' which ran a featured article on leptin. It was a 1990s study and the researchers were looking at mutant mice that had a tendency to grow fat. Such mice could eat non-stop without restriction. The researchers were interested in why these mice would not stop eating and subsequently become so fat. They found that a part of the genetic structure was destroyed, and identified a portion within the gene sequence responsible for the protein leptin. Here we see a fat cell, or 'adipocyte' and leptin is the substance released or secreted from adipocytes. When it is released the leptin suppresses the appetite for eating. However in the mutant mice, because the leptin-related portion of the gene sequence is damaged there is no limit to their eating and so they grow fat.

So we must ask how this relates to the accumulation of body fat. At the bottom of this rough drawing you can see the fat tissue. When eating too much, the fat tissue grows. As each cell gets larger the result is that leptin is released to act on the brain and suppress appetite. And so the cycle repeats. When not eating less leptin is released. So because of the leptin the body-fat ratio can be well-maintained and well-balanced.

However, despite elucidating this leptin mechanism, some mystery remains. For example, if we have such a mechanism why do people still become obese? That is another question. It may be that the modulation mechanism is damaged and that it is why it is not effective. As this suggests, we have not yet identified the entire scope of this mechanism. But talking generally about the upper central nervous system, while people have some control of their emotions their eating behavior is more about instinct. Maybe some of that behavior is being controlled by the upper CNS. For example, beyond the basic need to ingest calories to survive, eating is creating some additional value so that, even when you have satiated your appetite for calories, you still want to eat something. This is at odds with the original theory that when an appetite is well filled, the calorie intake negates any further appetite. However, humans can still retain an appetite which is being affected by upper CNS function.

So an idea was developed to use leptin as a drug to suppress this appetite. But studies showed that obese people already have a higher concentration of leptin in their blood which suggests that leptin is being secreted but that it is not working effectively enough.

Why is this so? Well, this problem is known as 'leptin resistance'. It seems that while leptin does affect the brain, the transmission of leptin to the brain has some limits. When normal people eat too much their leptin levels become slightly increased, which is effective for modulation. But when leptin levels increase significantly as a result of obesity, it may be that there is a limit or threshold on leptin functionality. Other research concludes that some kind of change may have occurred within the brain cells that receive signals from leptin. So once obesity occurs it is very difficult to reverse the situation. That is why prevention is very important.

So far I have been talking about human beings, but what about dogs? Here is one of my past studies and this is for the beagle breed. (Usually it is beagles that are used in experiments, which you may have often heard before). Data from 30 dogs was collected with varying levels of obesity. There is a method to measure the obesity level to identify the blood leptin concentration. When the obesity level is high, so the leptin secretion is higher. This was an experimental situation but I was also curious about dogs coming to clinics. So I looked at 166 dogs from various clinics in which there was a mixture of dog types, gender and ages. The more the dogs were obese, the higher their levels of leptin concentration. This slide shows the body condition score, indicating degree of obesity using a five-point scale. A reading of 3 is normal, whereas a 4 or 5 reading is obese. The more the dog is obese, the more the concentration of leptin, which is the same situation as in humans. Likewise, an obese dog has the same problem with appetite control as an obese human.

Another point regarding the causes of obesity is that there are some genetic factors at work although it is very rare to find situations where the genetic factors alone are the cause. Yes, there are some special cases in humans but, as I say, they are very rare. In the case of cats and dogs genetic diseases which cause obesity have not been found to date. Obesity symptoms can result from some endocrine diseases but they are neither severe nor frequent. So the question is whether we can ignore genetic factors? The answer is not certain. Again, in humans, the characteristics of individual genetic information are very important. An accumulation of several factors can lead to obesity. For instance, human metabolic levels are different among the individuals. Beta 3-adrerengic receptor mutation is famous as one of such causes. One-third of the Japanese population has this mutation so, compared to those without the mutation there is a tendency for these people to become obese even if they are consuming same calories.

So we must ask why such a mutation is still able to continue within the human body. Well, in times when food was less easy to find and people were generally half-starved, it was easier to survive if you had such a mutation. In the case of cats and dogs, we have not identified something like this. However, I have just proceeding pursuing this field of study so on some future occasion I may be able to report some new findings. Similar to humans having different kinds of racial difference, so dogs and cats have a degree of difference among their species. Therefore there is a possibility of a specific mutation in a specific breed which may differentiate that dog breed. That would be an interesting area for further study.

Well leptin levels in different kinds of dog have been analyzed, notably in Shih Tzu, dachshund, and some other breeds, and regardless of their type, there is a tendency to find higher leptin levels in the obese dogs. But in the case of miniatures dachshund it had a slightly different result. I am referencing a study that has only been done in Japan so I am not sure whether the same applies in other countries. This is because, in recent years, the popularity of miniature dachshund has increased rapidly in Japan. Therefore some diseases are appearing in Japanese dachshunds that are not very well known abroad. With such a background this may be a very special case study. Compared to other breeds of dogs, when the miniature dachshund becomes obese or puts on weight the increase in leptin is not so marked. This shows in the statistics also. The dachshund is a breed that puts on weight easily and we wonder if this might be because the lepin level does not increase enough which subsequently makes weight-gain easier. Of course we cannot say this definitively from these results alone but we are pursuing the research with this possibility in mind.

I have been talking about state of obesity in relation to leptin, but now let me go back to metabolic syndrome. Again, scientists are conducting these studies for human subjects, but we need to ask about dogs and cats. Looking at statistical studies made in Japan, the major causes of death in Japanese people are; cancer, heart disease and stroke. For cats and dogs they are; cancer, cardiac disease and renal disease.

So, due to longevity extension similar diseases began to be observed among dogs and cats living with humans. This is something reported from a media point of view, but as scientists, we need to examine more closely what kinds of cancer are becoming more frequent. In the case of humans, lung cancer, gastric cancer, and colon cancer make up the majority of cancers. But for dogs and cats, major malignant tumors are different. It is true that, in comparison to the past, more gastric cancers have been detected in recent years, but that they may be just the consequence of using endoscopy. But compared to cancers in humans gastric cancers are not the major cancers in cats and dogs. In terms of tumors, lymphoma is the most common in cats and dogs.

Instead, we should ask about cardiac diseases. In Japan, within humans, ischemic heart disease is quite common but, in dogs, it is mitral valve regurgitation and, in cats, cardiomyopathy, that are considered common diseases. Regarding these diseases humans are slightly in-between dogs and cats. Their types of disease and leading causes of death are slightly different.

Now, let me go back to the topic of metabolic syndrome within dogs and cats. One of the issues related to the metabolic syndrome is arteriosclerosis. This happens after plaque increases and accumulates. This causes blood

vessels to harden, a condition which limits blood flow and ischemia can occur. However this is not a regular cause of disease in cats and dogs. We don't see heart disease, common in humans, such as angina at our clinic. I cannot say that there are zero cases, but they are quite an exception. As I said before, we do see cases of cardiomyopathy or valve-related diseases which are more common than angina or myocardial infarction.

Now, let me talk about the other disease, diabetes. As I believe Dr. Sako will touch upon this issue I will not elaborate on my points. Generally speaking, we tend to simply compare humans and animals but there are of course differences among the other animal species – cats are different from dogs. So we have to focus specifically on individual species. In the case of dogs, the pancreas can be destroyed due to changes or impairments to the autoimmune system, or steroid hormones are the cause, or a factor of diseases. There are various causes and these trigger diabetes. In the case of cats, due to obesity we see that their insulin resistance increases which is closer to the situation of middle-aged humans growing obese and suffering from type 2 diabetes. Metabolic syndrome occurs along with type 2 diabetes and we see that the cat diabetes is quite similar to the human type 2 diabetes. In short, we see that dog diabetes is similar to human type 1 diabetes but that cat diabetes is very similar to human type 2 diabetes, although the complications are different. I was planning to explain about the mechanism of diabetes but it is not my focal point so, to avoid things becoming complicated, I will skip it. I will move on to the more important points as I need to make my conclusion about whether there is metabolic syndrome within cats and dogs.

The metabolic syndrome we see in humans does not exist among cats and dogs. However, when a dog begins to grow obese pancreatitis does occur which has been proven in studies. And we do see type 2 diabetes and hepatic lipidosis (in which fat accumulates within the liver) in cats. So if we call these conditions 'metabolic syndrome' then it is true that there is metabolic syndrome in dogs and cats. It is not only that when cats and dogs become obese the condition leads to diabetes and fatty liver (in cats) and pancreatitis. There is also a negative impact on the cardiovascular system and respiratory organs. There is also the impact on motor diseases, like joint disease in larger dogs. Once obesity occurs this puts an additional burden on the knees and joints, which makes the condition grow worse. And if there is no exercise therapy the situation is only exacerbated. There have been some recent studies on longevity and shortening life spans. In two groups of dogs, where one group was able to eat freely (without limit) and the other group eating only a restricted diet, comparative results showed the longer than 1-year life spans to be different. The same findings have been observed in monkeys, so evidence has begun to offer proof of shortening life spans. I also mentioned that it is very difficult to reverse the situation once obesity has set in but easy to control if you prevent the obesity in the first place. If you know that, then the obesity is not an issue of the tummy and your animal being cute, it is important to know that it includes all the life-span risk factors I have introduced. On that point I would like to conclude my talk. Thank you very much.