

MBP® Activates Osteoblastic Bone Formation and Regulates Osteoclastic Bone Resorption.

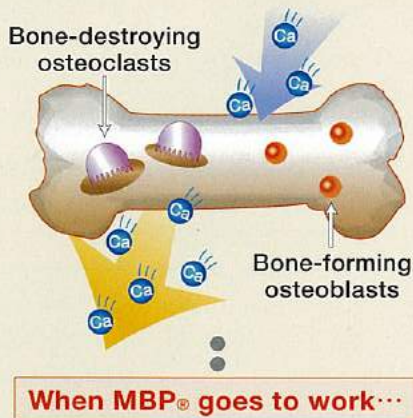


MBP® is a substance that works directly and/or indirectly on both osteoblasts and osteoclasts. At the same time as it activates osteoblastic bone formation, it suppresses the excess osteoclastic bone resorption. MBP® supports the formation of healthy bones.

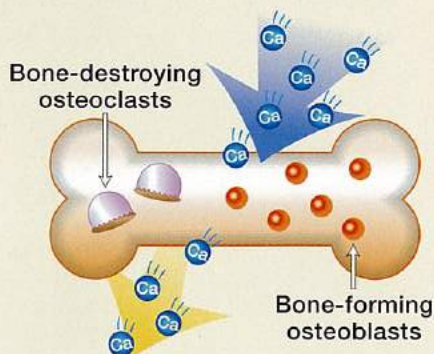
The key characteristic of MBP® is that it works directly and/or indirectly on bone cells.

MBP®'s most important characteristic is that it works directly and/or indirectly on both osteoblasts and osteoclasts. It makes bones receptive to calcium while at the same time deterring excessive dissolving of calcium and collagen out of bones. As a result, MBP® keeps our bones vital and healthy.

When a bone becomes unhealthy, osteoclasts function excessively and dissolve too much calcium.



Osteoblasts are activated, excessive osteoclast activity is inhibited, and the bone returns to health.



The calcium you ingest is wasted if it's not incorporated into your bones.

Because calcium cannot be synthesized within the body, it can only be obtained through meals or otherwise ingested. The calcium is absorbed from the intestine into the body and carried to the bones by the blood stream. However, even though calcium is ingested, if it does not adhere to and is not incorporated into the bones, it is expelled from the body in the urine or feces.

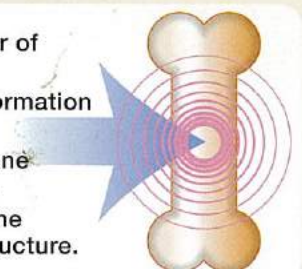
Revitalize your bones and effectively utilize the calcium you ingest. This is the key to building healthier bones.

The method of forming healthier bones we propose is based on the concept of avoiding wasting the calcium you ingest by storing it in your bones. The substance effective in promoting this is MBP®. Needless to say, ingesting an adequate supply of calcium and appropriate exercise are important in strengthening bones. However, that alone isn't enough. It is also important to thoroughly understand the process by which bones are reborn and to skillfully make use of MBP®, with its characteristic of working directly and/or indirectly on bone cells. We believe this will be the preferred method of forming healthy bones in the future.



The Functions of MBP®

- MBP® increases the number of bone-forming osteoblasts.
- MBP® promotes collagen formation by osteoblasts.
- MBP® inhibits excessive bone destruction by osteoclasts.
- MBP® maintains normal bone metabolism, tissue, and structure.





MBP[®] Improves Bone Metabolism for People in Each Age Group.

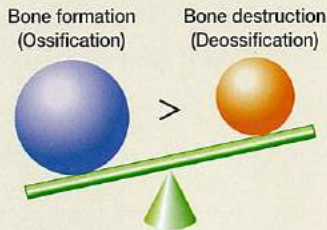
The following is an explanation of the functional relationship between bone-forming osteoblasts and bone-destroying osteoclasts for various age groups.



Growth Stage

Activate your bone development.

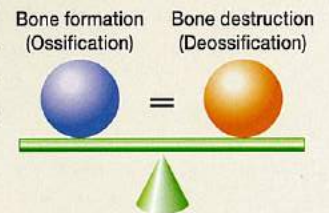
The growth period is a time when the metabolism is active and bones are vigorously formed, while at the same time destroyed. However, because the bone-forming function is more powerful than the bone-destroying function, the body grows larger. Diet and exercise are very important in promoting this growth function during this period. By the way, it is said that bone mass increases until about the age of twenty for the backbone and until about the age of thirty for the bones in the limbs.



Maturity period

Take care to keep strong bones for the future.

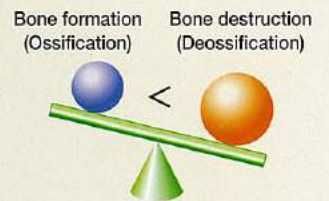
From the thirties onward, our bodies are fully grown and have reached peak bone mass. This is also a period when the bone-forming function and bone-destroying function are in balance. Accordingly, at this time of life a balanced diet is important for delaying the onset of future decreases in bone mass.



Old Age

Protect your bones from osteoporosis.

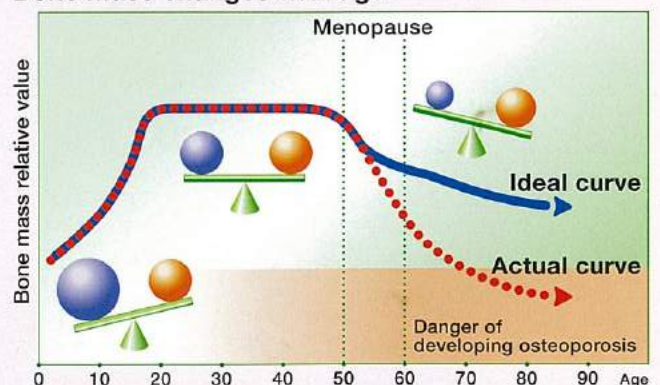
From the forties onward bone mass slowly decreases. This is a period when, on the whole, both the bone-forming function and bone-destroying function weaken, but the bone-destroying function is stronger. Osteoporosis sets in when this situation progresses to the level of illness. Consequently, it is extremely important to delay, as much as possible, the onset of bone mass reduction.



Why is osteoporosis prevalent among women?

The reason osteoporosis is prevalent among women is first and foremost that compared to men, women's skeletons are smaller, so the maximum bone mass stored in the body is lower. However, in addition to this, the female hormone estrogen exerts a major influence. Estrogen functions to inhibit the bone-destroying function of osteoclasts, but the excretion of this hormone nearly ceases with the onset of menopause. This causes excess activity of osteoclasts, and bone is increasingly destroyed, leading to osteoporosis. It is anticipated that MBP[®] will perform the role of controlling the excess activity of osteoclasts.

Bone mass changes with age.



FAQ about MBP®

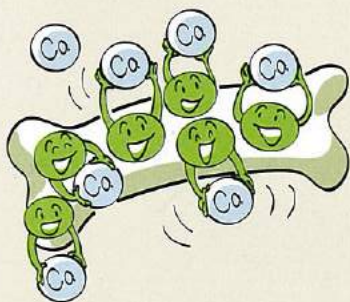


Q1 MBP® isn't necessary if I get lots of calcium, is it?

A If your bone cells don't function properly, ingested calcium isn't incorporated into your bones.

Calcium is merely the material used to form bones. It is osteoblasts that actually perform the task of forming your bones. Balance between osteoblasts and osteoclasts is important for the healthy rebirth of bones. No matter how much calcium you ingest, if your bones aren't receptive to the calcium, it isn't fully incorporated into the bones. Because MBP® activates the function of osteoblasts and suppresses excessive activity of osteoclasts, it constructs the foundation upon

which bones are built. MBP® is an important substance that promotes more effective utilization of the calcium you obtain from milk and other sources and the formation of healthy bones.

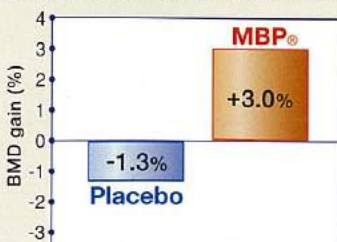


Q2 For how long a time should I drink MBP®?

A With MBP®, enhanced bone density has been confirmed after a period of six months. If possible, drink MBP® daily over a long period of time.

In tests in which people drank MBP® daily, improved bone metabolism has been confirmed after three months and enhanced bone density after six months. Because bone metabolism proceeds at an extremely gradual pace, it is important to drink MBP® over a long period of time. Furthermore, as your bones are reborn each day, you should try to drink MBP® daily.

MBP® increases radial BMD.



We studied the effects of daily intake of MBP® on BMD (bone mineral density) in 33 healthy adult women (from twenties to fifties). The mean of BMD at the distal end of the radius increased by 3% in the MBP® group after 6 months of ingesting 40 mg of MBP® a day.

(J. Yamamura et al.: 2002)

Q3 Isn't MBP® digested in the stomach?

A The activity of MBP® is resistant to digestion.

In experiments in which we artificially created MBP® in digested form, the digested MBP® worked on osteoblasts and osteoclasts in the same way as undigested MBP®. These findings suggest that even if MBP® is digested, the crucial components that work on the bones are delivered to the bones unchanged in nature. What's more, we found that the components of MBP® that work on bone cells are absorbed through the small intestine.



Reference

- Yamamura, J., Takada, Y., Goto, M., Kumegawa, M., and Aoe, S.: High mobility group-like protein in bovine milk stimulates the proliferation of osteoblastic MC3T3-E1 cells. *Biochem. Biophys. Res. Commun.*, 261, 113-117 (1999).
- Yamamura, J., Takada, Y., Goto, M., Kumegawa, M., and Aoe, S.: Bovine milk kininogen fragment 1·2 promotes the proliferation of osteoblastic MC3T3-E1 cells. *Biochem. Biophys. Res. Commun.*, 269, 628-632 (2000).
- Toba, Y., Takada, Y., Yamamura, J., Tanaka, M., Matsuoka, Y., Kawakami, H., Itabashi, A., Aoe, S., and Kumegawa M.: Milk basic protein: a novel protective function of milk against osteoporosis. *Bone*, 27, 403-408 (2000).
- Kato, K., Toba, Y., Matsuyama, H., Yamamura, J., Matsuoka, Y., Kawakami, H., Itabashi, A., Kumegawa, M., Aoe, S., and Takada, Y.: Milk basic protein enhances the bone strength in ovariectomized rats. *J. Food Chem.*, 24, 467-476 (2000).
- Takada, Y., Toba, Y., Aoe, S., Kumegawa, M., and Itabashi, A.: Milk basic protein (MBP) promotes bone formation and suppresses bone resorption. In: *Nutritional Aspects of Osteoporosis* (Burckhardt, P. Dawson-Hughes, B., and Heaney, R. P. ed.), pp. 141-153. Academic Press, New York, NY (2001).
- Aoe, S., Toba, Y., Yamamura, J., Kawakami, H., Yahiro, Kumegawa, M., Itabashi, A., and Takada, Y.: Controlled trial of the effects of milk basic protein (MBP) supplementation on bone metabolism in healthy adult women. *Biosci. Biotechnol. Biochem.*, 65, 913-918 (2001).
- Toba, Y., Takada, Y., Matsuoka, Y., Morita, Y., Motouri, M., Hirai, T., Suguri, T., Aoe, S., Kawakami, H., Kumegawa, M., Takeuchi, A., and Itabashi, A.: Milk basic protein promotes bone formation and suppresses bone resorption in healthy adult men. *Biosci. Biotechnol. Biochem.*, 65, 1353-1357 (2001).
- Yamamura, J., Aoe, S., Toba, Y., Motouri, M., Kawakami, H., Kumegawa, M., Itabashi, A., and Takada, Y.: Milk basic protein (MBP) increases radial bone mineral density in healthy adult women. *Biosci. Biotechnol. Biochem.*, 66, 702-704 (2002).
- Matsuoka, Y., Serizawa, A., Yoshioka, T., Yamamura, J., Morita, Y., Kawakami, H., Toba, Y., Takada, T., and Kumegawa, M.: Cystatin C in milk basic protein (MBP) and its inhibitory effect on bone resorption in vitro. *Biosci. Biotechnol. Biochem.*, 66, 2531-2536 (2002).