DOWNLOAD PDF ASSAY OF CALCIUM-REGULATING HORMONES

Chapter 1 : [PDF] Assay of Calcium-regulating Hormones Read Full Ebook - Video Dailymotion

Assay of Calcium-regulating Hormones. [Daniel D Bikle] -- The ability to measure accurately the hormones regulating calcium homeosta sis is the fundamental first step toward understanding the roles these hormones play in health and disease.

Xray of human chest area Photo Credit: Although the calcium circulating in your blood comprises less than 1 percent of your total body calcium, maintaining appropriate levels is vital for bone health and normal muscle and nerve function. Three principal hormones regulate blood calcium levels: Video of the Day Calcium Regulation Your blood calcium levels are influenced by regulatory processes that occur in your bones, gut and kidneys. Bones undergo constant remodeling. They are broken down by cells called osteoclasts, which release calcium into the bloodstream. Blood calcium can be taken up by other bone cells, called osteoblasts, which use the mineral to produce new bone. Blood calcium levels are also influenced by how much dietary calcium your small intestine absorbs and how much of the mineral your kidneys excrete. Parathyroid Hormone Located on the back of the thyroid gland in your throat, your parathyroid gland consists of four pea-sized nodules. When blood calcium levels drop, the parathyroid gland secretes parathyroid hormone. This hormone works to raise blood calcium levels by stimulating osteoclasts to break down bone and release calcium into the bloodstream. PTH also signals your kidneys to conserve calcium by reducing the amount excreted in the urine. The hormone also stimulates kidney production of the active form of vitamin D, which triggers increased calcium absorption from the gut. Low levels of PTH -- due to autoimmune disease or another cause -- can lead to abnormally low blood calcium. High levels of PTH -- most commonly caused by a parathyroid tumor -- cause excessively high levels of blood calcium. Vitamin D Vitamin D acts as a hormone in your body to help regulate blood calcium. This steroid hormone is so vital in maintaining calcium balance that its active form is sometimes referred to as calcitriol. Vitamin D is necessary for sufficient absorption of dietary calcium in your small intestine. A deficiency in vitamin D can cause low blood calcium, due to impaired calcium absorption. This can lead to weakening of the bones, as seen with the vitamin D deficiency conditions, rickets and osteomalacia. Vitamin D is produced in your skin with sun exposure, and is in some foods or from a supplement. Calcitonin Calcitonin, which is produced by your thyroid gland, serves to lower blood calcium levels. It counters the actions of parathyroid hormone. Calcitonin inhibits osteoclast function, slowing the breakdown of bone. By opposing the action of parathyroid hormone on the kidneys, it also increases excretion of calcium in the urine. High levels of calcitonin, which may be caused by a thyroid tumor, generally do not result in elevated blood calcium.

Chapter 2 : Hormones That Regulate Blood Calcium Levels | calendrierdelascience.com

The ability to measure accurately the hormones regulating calcium homeostaÂ- sis is the fundamental first step toward understanding the roles these hormones play in health and disease.

Calcium homeostasis in a healthy adult over 24 h. The skeleton is the major body storage site for calcium. Although the hormonal control of calcium fluxes is central to understanding of normal calcium homeostasis, Parfitt and co-workers 6 7 8 9 10 11 have also emphasized the importance of physico-chemical exchanges of calcium between the bone fluid and the ECF. The bone fluid is rich in calcium because it is in equilibrium with the mineral phase of bone at the bone surface. The exchanges between the bone fluid and the ECF may be important in determining the set point mean concentration of serum calcium at steady state and error correction by which serum calcium is returned to the set point and corrected by oscillations in the ionized calcium concentrations about this mean. The relative importance of this exchange mechanism has been underappreciated. Neuman showed almost 40 years ago that there is a special bone fluid that is analogous to the cerebrospinal fluid. This bone membrane functions to keep calcium in the ECF and out of the bone the ECF is supersaturated with calcium compared with both the bone fluid and the crystalline surface of bone. The hormonal mechanisms that might control calcium fluxes across the bone membrane are unknown at present, as are any possible influences on these fluxes by disease states such as the hypercalcemia of malignancy or primary hyperparathyroidism. However, it is possible that these fluxes buffer fluctuations in ECF calcium caused by, for example, dietary calcium loads or calcium entry from bone destruction caused by malignancy. For example, these fluxes may be important in determining set point. They could also be important in returning plasma calcium to the steeping error correction after a calcium load. Hormonal Effects on Calcium Homeostasis Blood ionized calcium concentrations are remarkably stable in healthy individuals because of the homeostatic system involving the actions of the three calciotropic hormones on the target organs of bone, gut, and kidney, and possibly also on fluxes between the bone canalicular fluid and the ECF mentioned above. Normal calcium homeostasis is primarily dependent on the interactions of PTH, 1,25 OH 2D3, and calcitonin on these organs to maintain the ionized calcium concentration within a very narrow range. Other factors also influence calcium fluxes, although current evidence suggests that only these three hormones are under negative feedback control. Secretion of PTH is highly dependent on the ionized calcium concentration and represents a simple negative feedback loop. The serum PTH concentration decreases as the serum calcium concentration increases, although PTH secretion is not entirely suppressible The calcium-sensing receptor that mediates this negative feedback has recently been cloned from bovine parathyroid cells This G-protein-linked receptor is mutated in the disorders of familial hypocalciuric hypercalcemia 17 , neonatal severe hyperparathyroidism, and autosomal dominant hypocalcemia 18 Synthesis of PTH is likely maximal under normal physiologic conditions because parathyroid cells exposed to hypercalcemic conditions in vitro display a decrease in mRNA for PTH, whereas those exposed to hypocalcemic conditions do not show such an increase Active vitamin D metabolites decrease PTH synthesis in vitro and in vivo 21 22 as well. The biological actions of PTH include a stimulation of osteoclastic bone resorption and release of calcium and phosphate from bone, b stimulation of calcium reabsorption and inhibition of phosphate reabsorption from the renal tubules, and c stimulation of renal production of 1,25 OH 2D3, which increases intestinal absorption of calcium and phosphate. The PTH receptor has recently been cloned and found to be a member of the large family of receptors that contain a seven transmembrane-spanning domain and work through activation of G-proteins PTH metabolism is complex and produces several fragments of varying biological and immunological reactivity. Intact PTH is cleared rapidly by kidney and liver 25 26 Hepatic Kupffer cells take up intact PTH and degrade it into very small peptides as well as cleave it into discrete fragments that are released into the circulation 28 29 The released carboxy-terminal fragments circulate considerably longer than the intact hormone, mainly because they are cleared exclusively by glomerular filtration 28 31 The complex metabolism and circulating heterogeneity of PTH are likely reasons for the difficulty encountered in developing good PTH assays. Highly sensitive and specific immunoradiometric assays for intact PTH are now

widely available This factor is now known to be expressed by many squamous cell carcinomas and has also been described in T-cell lymphomas that present with humoral hypercalcemia It is a amino acid peptide and shares considerable homology with PTH in the first 13 amino acids. It binds to and activates the PTH receptor, and this is presumably the reason it mimics the biological effects of PTH on bone, kidney, and the gut. It stimulates osteoclastic bone resorption and promotes renal tubular calcium reabsorption in similar concentrations to that of native PTH In some models of hypercalcemia associated with increased PTH-rP, hypercalcemia can be reversed by passive inoculation with neutralizing antibodies to PTH-rP RIAs have been developed for PTH-rP, although these assays have not shown a perfect relationship between the presence and severity of hypercalcemia and expression of the protein 35 42 It is now clear that PTH-rP has a pathophysiological role not just in hypercalcemia but also in local osteolysis. Immunohistochemistry has been used to demonstrate that there is increased expression of PTH-rP in bone sites compared with either soft tissue metastases or primary tumors in patients with carcinoma of the breast This has been shown experimentally by inoculation of the human breast cancer cell line MDA-MB into the left cardiac ventricles of nude mice. Osteolytic lesions caused by metastasis occur over the following 4â€”6 weeks, and there is an increase in PTH-rP expression in the tumor cells that metastasize to bone. When tumor-bearing nude mice are treated with neutralizing antibodies to PTH-rP, not only is there a decrease in the development of the osteolytic bone lesions, but there is also a decrease in the tumor burden in bone The physiological role of the PTH-rP remains unclear. It probably has no regulatory effect on calcium homeostasis under physiological conditions. It is produced in healthy skin cells as well as in amniotic cells, and it may have effects on epithelial cell replication and on smooth muscle contraction during labor It is also expressed by lactating breast tissue and is present in large amounts in breast milk. However, most recent interest has focused on its potential local effects in cartilage differentiation. PTH-rP knockout experiments performed by introducing the null-mutation into the germ line of mice have shown that the mice have died before birth of an abnormality of the rib cage that causes impaired respiration These abnormalities are caused by an enhanced cartilage cell differentiation and normal ossification in the rib cage. Thus, PTH-rP is a naturally occurring and essential inhibitor of cartilage cell differentiation, and its absence leads to abnormalities at the growth plate. Overexpression experiments using transgenic mice in which PTH-rP expression is targeted to cartilage cells by use of the type II collagen promoter show a marked delay in endochondral ossification 46 and also demonstrate cartilage abnormalities Its effects on cartilage cells seem to be mediated by Indian hedgehog protein produced by prehypertropic cartilage cells in the growth plate 47 Two PTH receptors have been identified. The importance of this second PTH receptor is not clear, and there are many important questions that need to be addressed. These include the effects of PTH-rP on this receptor and whether these are identical to those of PTH, whether this receptor can explain some of the controversial non-bone effects of PTH that have been described for many years such as those on the vascular system, what the signal transduction pathway that is connected to this receptor is, and finally whether this receptor is related to the anabolic response of PTH. Early studies suggest the receptor is not as responsive to PTH-rP as it is to PTH and that it may mediate its effects through cAMP and intracellular calcium signal transduction pathways The ionized calcium concentration is the most important regulator of calcitonin secretion Increases in ionized calcium produce an increase in calcitonin secretion, and conversely, a fall in the ambient calcium concentration inhibits calcitonin secretion. Gastrointestinal peptide hormones, gastrin in particular, are potent calcitonin secretogogues. This likely is responsible for increased calcitonin secretion after meals, but the physiologic relevance of this observation remains unclear. Pentagastrin, a gastrin analog, is used as a provocative stimulus to determine the capacity of a patient to secrete calcitonin The precise biological role of calcitonin in the overall schema of calcium homeostasis is uncertain. Calcitonin directly inhibits osteoclastic bone resorption 54 , and the effect is rapid, occurring within minutes of administration. This inhibition is accompanied by the production of cAMP 55 as well as an increase in cytosolic calcium 56 in the osteoclast and leads to contraction of the osteoclast cell membrane These effects are transient and likely have little role in calcium homeostasis chronically, although they may be important in short-term control of calcium loads. Clinical observations support the notion that calcitonin has little chronic effect because neither calcitonin-deficient patients athyroid nor patients with medullary thyroid cancer and

excess calcitonin production experience alterations in calcium homeostasis. The calcitonin receptor has been cloned 58 and is structurally similar to the PTH receptor in that it also has seven transmembrane domains. Calcitonin is metabolized in minutes in the circulation, predominantly in the kidney 1. The calcitonin receptor exists in several isoforms, and its expression seems to be influenced by ambient concentrations of calcitonin itself. This may be the reason for down-regulation of the receptor and the escape phenomenon that occurs in the continued presence of calcitonin The vitamin D precursor previtamin D3 is either ingested in the diet or synthesized in the skin from 7-dehydrocholesterol through exposure to sunlight Hydroxylation occurs in the liver at the C position to form hydroxyvitamin D, the substrate for the more potent metabolite, 1,25 OH 2D3. The only other known important extrarenal sites of 1,25 OH 2D3 production are in the placenta and granulomatous tissue 65 66 It also increases bone resorption 68 and enhances the effects of PTH in the nephron to promote renal tubular calcium reabsorption. It is a powerful differentiation agent for committed osteoclast precursors 69 70 , causing their maturation to form multinucleated cells that are capable of resorbing bone. By these actions, 1,25 OH 2D3 provides a supply of calcium and phosphate available at bone surfaces for the formation of normal mineralized bone. Whether 24,dihydroxyvitamin D3 has effects on bone metabolism has been a controversial issue for years. Many people have believed it to be biologically inert. However, recent studies in null-mutant mice in which the hydroxyvitamin D hydroxylase gene is deleted throw doubt on this notion Although the heterozygotes are apparently normal, approximately one-half of the homozygotes die before weaning, apparently because of hypercalcemia associated with nephrocalcinosis. Although the bone histology is normal in the first generation of homozygotes, the second generation show an accumulation of osteoid tissue at sites of intramembranous ossification, such as in the calvaria, clavicle, mandible, and periosteal surface of long bones. These studies suggest that 24,dihydroxyvitamin D3 may play an important role in normal intramembranous bone formation. Recently, there have been further clarifications of the receptor mechanisms and response elements in target genes for 1,dihydroxyvitamin D. The gene that has been used most frequently for studying transcriptional effects of the vitamin D receptor is the osteocalcin gene, which has provided a wealth of information. It is apparent that the vitamin D receptor functions as a transcription factor like other members of the steroid hormone superfamily and causes effects on target genes by forming a heterodimer with the retinoic acid receptor, and this is responsible for the mediation of its effects on gene expression

Chapter 3 : An Overview of the Parathyroid - The Calcium-regulating Gland that Helps Keep Bones Healthy

The ability to measure accurately the hormones regulating calcium homeostaÂ- sis is the fundamental first step toward understanding the roles these hormones play in health and disease. Techniques for such measurements have only been available for the past 10 years or so and remain in a state of rapid development.

This article has been cited by other articles in PMC. Abstract Background Very little is known of the regulation of the function of human osteoclasts, largely due to the virtual impossibility of obtaining human osteoclasts ex vivo. However, the assays at present available do not distinguish clearly between the distinct effects of agents on differentiation and function. Materials and methods We developed a novel assay for resorptive function of human osteoclasts that minimizes inter-assay variability by using each culture as its own baseline, and that minimizes the confounding effects of agents on differentiation by assessing resorptive function over a short test period. In this assay, the development of resorptive activity is monitored in sample cultures. When resorption is underway, bone resorption measured as the release of the C-terminal telopeptide degradation product of type I collagen CTX-I into the supernatant is compared before vs after incubation for 1â€”24 h in test agent. Results Using this assay, we found that changes in bone resorption could be detected using substantially fewer cultures per variable. Moreover, we could detect effects of agents on resorption within 1 h of addition, a time sufficiently short that a change in release is likely to reflect an effect on function rather than on differentiation. Conclusion The assay makes it possible to distinguish the effects of agents on osteoclastic function, independent of their effects on differentiation. Background The maintenance of skeletal integrity depends on continual resorption of bone by osteoclasts and its replacement by osteoblasts. Recently, there have been considerable advances in our understanding of the mechanisms through which osteoclast formation is regulated [1 - 3]. In contrast, little is known of the mechanisms that modulate their activity once formed, even although this is a major component of the regulation of bone resorption. Thus, after systemic administration of hormones such as PTH or CT, osteoclasts show morphological evidence of an increase or decrease in activity, with a corresponding change in plasma calcium concentration, within 30 min, while a change in osteoclast number is not detectable until 24 h later [4]. This shows that bone resorption is regulated not only through modulation of the number of osteoclasts but also by modulation of the resorptive activity of existing osteoclasts. It seems likely that agents exert differential actions on these distinct processes. It is virtually impossible to obtain human osteoclasts ex vivo with which to address this question. However, although such culture systems provide powerful insights into the regulation of osteoclastic differentiation, they do not clearly distinguish between the effects of agents on differentiation and function. For example, resorption of bone slices in such culture systems is typically observed after 14â€”21 days of incubation [7 - 10]. If a putative resorption modulator is added to such cultures for a brief period, effects on resorption, classically measured as the area of bone surface excavated, will be observed against a baseline of prior resorption; and if the modulator is added over a longer period, it will be difficult to distinguish effects on function from those on differentiation. Recently, it has become possible to measure bone resorption as the release into culture supernatants of products of bone solubilization, the concentration of which has been shown to correlate with bone resorption [11]. This approach has the advantage that the amount released reflects the amount of bone resorbed since the last change of culture medium. This avoids the results being masked by the baseline of prior resorption. However, even in such assays, bone resorption is measured over a period of 3 days [12 , 13], so that an unknown and potentially substantial component of an observed change in resorptive activity might have been due to an effect of the test agent on differentiation rather than function. The difficulties in the interpretation of resorption data mentioned above are compounded by the length of time it normally takes for osteoclastic differentiation to occur: This variability increases the number of cultures required per variable, and because relatively small numbers of monocytes are available from a given donor, the number of variables that can be studied in each experiment is in practice severely limited. We therefore developed a novel assay that minimizes the confounding effects of agents on differentiation by measuring resorption over a shorter period; and that minimizes inter-culture variability by using each culture as its own

baseline. In this assay, sample cultures are inspected to monitor the development of actively resorbing osteoclasts. When resorption is underway, release of products of bone resorption is compared before vs after incubation for 1â€”24 h with test agent. Using this approach, we found that changes in bone resorption could be detected using substantially fewer cultures per variable; and that effects of agents on resorption could be detected within 1 h of addition, a time sufficiently short that a change in release is likely to reflect an effect on function rather than on differentiation. Salmon CT, E64 and all remaining reagents were from Sigma unless otherwise stated. The blood was layered over Histopaque and centrifuged for 30 min at g. Bone slices were then inspected by light microscopy for the presence of osteoclasts and excavations see Fig. When excavation was deemed sufficient, the remaining cultures were subjected to the osteoclast resorption assay.

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Chapter 4 : A novel assay for analysis of the regulation of the function of human osteoclasts

Assay of Calcium-regulating Hormones by D. D. Bikle The ability to measure accurately the hormones regulating calcium homeostaÂ- sis is the fundamental first step toward understanding the roles these hormones play in health and disease.

There are four parathyroid glands, and they are each about the size of a grain of rice. The parathyroid glands are four small glands that have the sole purpose of secreting parathyroid hormone to regulate the calcium level in our bodies. The parathyroid essentially helps the nervous and muscular systems function properly. Calcium is the primary element that causes muscles to contract, and calcium levels are very important to the normal conduction of electrical currents along nerves. Anatomy of the Parathyroid Glands The four parathyroids are typically found on the back side of the thyroid. Although the parathyroids are very close to the thyroid gland anatomically, they have no related function. Parathyroid Hormone Parathyroid hormone PTH has a very powerful influence on the cells of your bones by causing them to release their calcium into the bloodstream. PTH regulates how much calcium is absorbed from your diet, how much calcium is excreted by your kidneys, and how much calcium is stored in your bones. PTH increases the formation of active vitamin D, and it is active vitamin D that increases intestinal calcium and phosphorus absorption. Diseases and Disorders of the Parathyroid When the parathyroid releases too much or too little PTH, it adversely affects your body in a variety of ways. Below are common diseases and disorders associated with the parathyroid glands: The most common disease of parathyroid glands is hyperparathyroidism, which is characterized by excess PTH hormone, regardless of calcium levels. In other words, the parathyroid glands continue to make large amounts of PTH even when the calcium level is normal, and they should not be making the hormone at all. Hypoparathyroidism is the combination of symptoms due to inadequate parathyroid hormone production. This leads to decreased blood levels of calcium hypocalcemia and increased levels of blood phosphorus hyperphosphatemia. This is a rare condition and most commonly occurs because of damage or removal of parathyroid glands during parathyroid or thyroid surgery. When one of the parathyroid glands is overactive, it releases too much PTH hormone. This causes your bones to release calcium constantly into the blood stream. Without enough calcium in your bones, they lose their density and hardness. Osteoporosis is characterized by this loss of calcium and bone density. The parathyroid glands have a single responsibilityâ€”regulating calcium levels. The glands are important members of endocrine system, but they are also integral to the proper functioning of the nervous and muscular systems.

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Sensitive parathyroid hormone (PTH) radioimmunoassays appeared in the early s, and with them came a whole new appreciation for the prevalence and implications of hyperparathyroidism, primary or secondary, in the popuÂ- lation.

Chapter 6 : - NLM Catalog Result

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Chapter 7 : Hormonal Control of Calcium Homeostasis | Clinical Chemistry

Cet ado transsexuel reÃ§oit en cadeau sa premiÃ¨re dose d'hormones et se met Ã pleurer.