IDEA/HYPOTHESIS

OSTEOPOROSIS IN WOMEN: SEMINAL FLUID COMPOUNDS ABSORBED THROUGH MUCOSAL TISSUES HELP PROTECT AGAINST & REMEDIATE BONE LOSS

By
Anthony G. Payne

Human seminal fluid contains hormones and other compounds that readily penetrate mucosal membranes and enter the recipient's circulation. Many of these exert a beneficial influence on human physiology including bone cycling (formation and breakdown), even in very small amounts. It is hypothesized that protection against and slowing of bone loss in women rises in step with exposure to male seminal fluid.

Main Body

Seminal plasma contains a plethora of powerful bioactive compounds. According to published analyses this includes but is not limited to these:

- The steroid hormone cortisol which according to immunoassay estimates is about 60% of random levels in blood serum (Brotherton, 1990a)
- Transcortin or corticosteroid-binding globulin exists in human seminal plasma at concentrations approximately 10% of levels in blood serum (Brotherton, 1990a)
- Androgens including testosterone are found in relatively high concentration in human semen, e.g., testosterone at approximately 559 pg/ml (Ney, 1986), with testosterone and dihydrotestosterone significantly higher in men with sperm in their ejaculate than in men who have had a vasectomy (Asch et al., 1984). A 1987 study found mean amounts of total testosterone ranged from 25.1 +/- 7.4 to 32.5 +/- 12.2 ng/100 mL, and those of the free hormone from 7.0 +/- 2.8 to 7.9 +/- 2.3 ng/100 mL.
- Human semen also contains the female hormones estrone and estradiol (Asch et al., 1984), with the former at levels twice that although the latter (Ney, 1986). At least one study found the levels of estradiol in seminal plasma to be significantly higher than what was found in their blood plasma (Luboshitzky, Shen-Orr, and Herer, 2002)
- Human semen contains 220 IU/ml luteinizing hormone which is actually the highest concentration of any hormone in same. Follicle-stimulating hormone is also present albeit in a much lesser concentration (Ney, 1986).

- At least thirteen (13) different prostaglandins have been found in human semen (Homberg and Samuelsson, 1966). At least some of these such as E1, E2 and F2 are rapidly absorbed through vaginal tissues (Sandberg et al., 1968).
- The "trust hormone" oxytocin is found in the seminal plasma of normal men and is present in slightly lower concentrations in men with poor semen quality as well as those who have had a vasectomy.
- Vasopressin is also found in male seminal plasma.
- Prolactin at approximately 86ng/ml is present in human seminal plasma (Ney, 1986).
- Calcitonin is present in human seminal plasma.
- A thyrotropin-releasing-hormone-like peptide has been found in human semen (Gkonos et al., 1994; Khan et al., 1992; Khan Sz Smyth, 1993; Pekary et al., 1990)
- Serotonin has been found in human seminal plasma.
- Enkephalins (natural opioids) are present in human semen.

These and many more compounds are discussed in R. L Burch and G. Gallup, Jr.'s "The psychobiology of semen" (August 2006), in Steve M. Platek and Todd Shackelford's "Female Infidelity and Paternal Uncertainty: Evolutionary Perspectives on Male Anti-Cuckoldry Tactics" (Cambridge University Press. pp. 141-172). They also point out that:

- Testosterone is not only absorbed in the vagina but at higher levels than testosterone applied transdermally. In fact, about 63% of the testosterone applied vaginally was absorbed (Wester, Noonan, 8r Maibach, 1980).
- Treatment with androgens even in very low doses can increase sexual desire in some human females (Carter, 1992).

In addition to the impact of androgens on recipient sexual desire and perhaps responsiveness, many researchers have suggested that orally or vaginally introduced semen lessens depression, anxiety and pain, enhances pair bonding and lowers blood pressure.

However, it appears that no studies have been published (on PubMed, July 2012) that explore the possible role of semen in protecting recipients from bone loss and perhaps also promoting osteogenesis. This forms the heart of the hypothesis I am advancing in this paper: Namely, that bone loss in women (and perhaps also homosexual and bisexual men) will be lower in those exposed to semen and that the degree of loss will, after correcting for hormonal, dietary and lifestyle factors, correlate with frequency of exposure.

Bone Genesis, Preservation & Loss: A Biologic Balancing Act

Bone is deposited by osteoblasts and resorbed by osteoclasts. One of the major mechanisms that result in osteoporosis is an imbalance in bone deposition-bone resorption (Bone turnover). Bone turnover, in turn, is influenced by the interplay of many factors such as a deficiency of vitamin D and calcium (which leads to poor bone deposition) as well as calcium metabolism and hormones such as estrogen.

When calcium levels are too low the body responds by secreting parathyroid hormone (PHT) which increases bone resorption resulting in release of bone calcium. Calcitonin, which is secreted by the thyroid gland, reduces blood calcium offsetting or opposing the effect of PTH (albeit the normal amount present in humans is not deemed to play a significant role in calcium homeostasis). Calcitonin is prescribed as a treatment for osteoporosis.

At least some evidence indicates that thyroid stimulating hormone (TSH) may reverse bone loss.

Testosterone, too, plays a role in bone integrity. Various studies have established that as testosterone levels drop in aging men their bone density decreases, something that can be offset to a certain degree by augmenting the hormone, e.g., transdermal patches, injections, etc. Testosterone levels in women, though lower than those of men, nonetheless impact bone density when deficient.

Other players in promoting healthy, strong include human growth hormone, vitamin K2 (especially menaquinone-7 which plays a role in shuttling calcium from blood to bone), magnesium, phosphorus, and boron.

Bone formation and density is favorably influenced by weight bearing exercise and undermined by being sedentary, inadequate dietary intake of calcium, magnesium, vitamin K2 and others, smoking, alcohol abuse, use of certain drugs (both licit and illicit), and much more.

Hypothesis: Hormones and other biologically powerful compounds in semen prevents bone loss and promotes osteogenesis in concert with frequency of exposure

As was signaled in the first section (under “Main Body) human semen contains a wealth of hormones and other compounds, many of which are readily absorbed through mucosal tissues and exert an influence on many different aspects of human biology including mood and possibly fertility. The testosterone, estradiol, calcitonin and oxytocin in seminal plasma all impact bone metabolism in favorable ways and as such one would expect that increases in them (especially testosterone) that reach biological significance, i.e., either pushing normal levels higher, remediating subclinical deficiencies where these exist or acting in concert with other bodily hormones and compounds that impact bone cycling) would tend to bolster recipient bone metabolism processes that prevent bone loss and favor bone-building.

However, when one looks closely at the quantities of testosterone, estradiol, calcitonin and oxytocin in the average male ejaculate it becomes clear that the amount of each is very miniscule.

Testosterone

The normal range of testosterone for women is 30 to 95 nanograms per deciliter (ng/dL) and 300 to 1,200 ng/dL for men, according the NIH (National Institutes of Health). Women tend to have an average of 70 ng/dl around age twenty which drops to 35 ng/dl after menopause.

Physicians have been prescribing low-dose testosterone for many years for a wide variety of conditions including depression and certain forms of heart disease in women. The dose in one small eight week pilot study (2009) for treatment-resistant depression in nine women was 300 micrograms per day. A recent (2012) study that tested the pharmacokinetics of sublingual doses of testosterone in healthy premenopausal women found that free and total testosterone increased in a dose-dependent fashion.

The quantity of testosterone in human seminal plasma is approximately 559 picograms/ml. The average male ejaculate is 3.2 +/- 1.4 ml which – using 3.2 ml -- translates to 1788.8 picograms or 0.0017888 micrograms total. Even if all of this were absorbed through recipient mucosal membranes and reached the systemic circulation (unlikely) the dose is admittedly quite low in comparison with therapeutic doses used by physicians. For instance, in the depression study cited above 300 micrograms per day was utilized.

Estradiol

A 1987 study found that the values for estradiol (E2) in semen from normozoospermic men were 10.5 +/- 4.4 to 11.2 +/- 4.5 pg/mL and 2.3 +/- 1.1 to 3.2 +/- 2.6 pg/mL in semen collected from oligozoospermic men. Estradiol levels in women vary with age and in premenopausal women with their menstrual cycle, something depicted in this Wikipedia chart: http://en.wikipedia.org/wiki/Estradiol#Measurement. Using the lowest figure above – 10.5 pg/mL (+/- 4.4) x 3.2 ml (average ejaculate in mL) gives a range of 19.52 to 47.68 picograms. This amount is very small compared to the serum range per mL of E2 in premenopausal as well as postmenopausal women.

Calcitonin

In a 1989 Israeli study researchers quantified the amount of beta-E and calcitonin in samples of seminal plasma and isolated pools of sperm from semen samples collected from 36 men (normospermic, oligozoospermic, and azoospermic). The mean level of calcitonin in plasma calculated for all samples was 754 +/- 397 pg/ml. Using the lower figure (754 – 397) and 3.2 mL (average male ejaculate), this translates to 1142.4 picograms calcitonin total.

In a 1998 paper the mean value of calcitonin in normal males and females was found to be 2.26 and 1.33 pg/ml respectively using an improved version of the chemiluminescent enzyme immunoassay (CLEIA) method.

If all 1142.4 picograms of calcitonin were absorbed and reached the blood stream the increase per mL of blood would be 0.2253 picograms.

Oxytocin

Dutch researchers carried out a 1998 study in which oxytocin in seminal plasma was measured by radioimmunoassay in semen samples from 3 groups of patients: Those with poor semen quality, those who had had vasectomies, and controls. They found that oxytocin levels did not differ those with poor semen quality (II: 1.66 +/- 0.91 pg/mL; n = 11), vasectomized patients (III: 1.28 +/- 0.65 pg/mL; n = 11) or in control patients (I: 1.72 +/- 0.78 pg/mL; n = 10). If one uses the lowest figure (1.28 – 0.65) which is 0.63 pg/l x.3.2 mL (average male ejaculate), this translates to 2.02 picograms oxytocin total.

In a paper published in 2011 researchers found that serum oxytocin levels in 16 healthy women (controls) averaged 110.6 pg/ml compared to 20 postmenopausal severely osteoporotic women (50.2 pg/ml).

If all 2.02 picograms oxytocin in a single ejaculation reached the recipients bloodstream the increase per milliliter of blood would be 0.000398422 picogram.

Given the relatively small quantities of testosterone, estradiol, calcitonin and oxytocin that likely reaches the recipients bloodstream following sufficient contact with semen it seems unlikely that these significantly impact bone metabolism. However, it is conceivable that the combination of these and other bioactive molecules in semen augment and even amplify the activity and/or impact of the constellation of hormonal and non-hormonal (including dietary) players present in women that prevent bone loss and remediate same. And in keeping with this, bone loss should be significantly less in women who have the greatest exposure to semen (oral, vaginal, anal deposition and retention) on a regular basis (especially during peak bone formation years) versus those who do not.

One way to scientifically test this would be to do a longitudinal study in which (a) research(ers) collect and compare data on bone loss from fit, healthy women of various body types (endomorphic, ectomorphic, mesomorphic) from puberty through menopause and beyond, segregated with respect to frequency of exposure (receipt and retention of semen), i.e., those who do so at average monthly rates, as well as those who are significantly below and above this. This data would be compared and contrasted to that obtained from matched controls with no exposure to semen whatsoever (or extraordinarily rare exposure).

Hopefully some enterprising young scientist in a position to flesh this out and run with this hypothesis will do so.

Other papers and articles by Choctaw Doc on sexuality-related topical issues and subjects:

Sex: We feed but can we tame the bulldog? (Examiner article)

Improving Male Sexual Responsiveness & Performance

Sexual Addiction Among Women Seeking "Well-Endowed" Male Partners: Results of a Survey (pdf)

Simple E.D. Gadgets making drugs a thing of the past

Study reveals that masturbation reduces odds of developing prostate cancer

"Prostate Massage Methods" (LiveStrong.com)

ADDITIONAL READING ON BONE FORMATION & LOSS

http://www.sciencedaily.com/releases/2007/03/070323171448.htm

How Estrogen Protects Bones

ScienceDaily (Mar. 23, 2007) — Researchers at the University at Buffalo have described a novel pathway by which estradiol, the primary estrogen in humans, aids in maintaining bone density, a function critical to avoiding osteoporosis.

It is well known that estrogen is essential for healthy bone, and that when the production of estrogen is reduced, as occurs normally in postmenopausal women and pathogenically after exposure to radiation or chemotherapeutic drugs, bones become brittle and break easily. However, the mechanisms involved aren't clearly understood.

The new study found that one way estradiol helps to maintain bone density is by stopping the activation of an enzyme known as caspase-3. Also called the executioner caspase, caspase-3 is the central player in initiating the process of apoptosis, or programmed cell death of osteoblasts, the bone cells that aid in the growth and development of new bone and teeth.

Results of the study will be presented at the International Association of Dental Research meeting in New Orleans.

Peter G. Bradford, Ph.D., senior author on the study said of the results: "Basic and clinical studies have shown that estrogens can prevent both bone loss and reduce the incidence of bone fractures. Our research at the molecular and cellular level suggests that the underlying basis of this protective effect of estrogens involves the prevention of apoptosis in osteoblasts and that the key event in this prevention is the inhibition of caspase-3 activity."

Bradford is an associate professor of pharmacology and toxicology in the UB School of Medicine and Biomedical Sciences and associate professor of oral biology in the UB School of Dental Medicine. Kenneth V. Gerace, a third-year dental student in his laboratory, is first author on the study.

To determine the effect of estradiol on caspase-3 activity, one group of human osteoblasts was treated with estradiol for 24 hours and another group was not. Both groups then were exposed for 24 hours to a drug called etoposide, a cancer chemotherapeutic drug that promotes apoptosis.

Results showed that caspace-3 activity decreased in cells treated with estrogen, but increased in cells not treated with estrogen.

"These findings support our hypotheses that the anti-osteoporotic effects of estradiol may result in part from its anti-apoptotic effects on osteoblasts," said Bradford.

"We now are investigating the biochemical mechanisms that mediate the estrogen-dependent inhibition of caspase-3 activity in osteoblasts and whether other pharmacological or nutritional agents might mimic or aid this action of estradiol."

Brian G. Chrzan, a UB orthodontic resident and oral biology doctoral candidate, also contributed to the research.

Fellowship support for Gerace was provided by a research training grant from the National Institutes of Health.

J Cell Biol. 2010 Oct 4;191(1):7-13.

The two faces of serotonin in bone biology.

Ducy P, Karsenty G.

Source

Department of Pathology and Cell Biology, Columbia University Medical Center, New York, NY 10032, USA. pd2193@columbia.edu

Abstract

The serotonin molecule has some remarkable properties. It is synthesized by two different genes at two different sites, and, surprisingly, plays antagonistic functions on bone mass accrual at these two sites. When produced peripherally, serotonin acts as a hormone to inhibit bone formation. In contrast, when produced in the brain, serotonin acts as a neurotransmitter to

exert a positive and dominant effect on bone mass accrual by enhancing bone formation and limiting bone resorption. The effect of serotonin on bone biology could be harnessed pharmacologically to treat diseases such as osteoporosis.

PMID: 20921133

http://www.ncbi.nlm.nih.gov/pubmed/20921133

http://www.ncbi.nlm.nih.gov/pubmed/21123937

Clin Calcium. 2010 Dec;20(12):1850-956.

[Control of bone remodeling by nervous system. The role of serotonin in the regulation of bone metabolism].

[Article in Japanese]

Inose H.

Source

Department of Genetics and Development, Columbia University, NY, USA.

Abstract

There is increasing evidence for a contribution of serotonin to the regulation of bone metabolism. In the periphery, gut derived serotonin (GDS) regulates osteoblast proliferation and bone formation. In the brain, brain derived serotonin regulates bone mass through sympathetic nervous system. In addition, inhibition of GDS biosynthesis can treat osteoporosis in ovariectomized rodents by increasing bone formation. The emerging evidence has suggested that inhibiting GDS biosynthesis could become a new anabolic treatment for osteoporosis in humans.

PMID: 21123937

http://www.ncbi.nlm.nih.gov/pubmed/18583541

Stem Cells. 2008 Sep;26(9):2399-407. Epub 2008 Jun 26.

Oxytocin controls differentiation of human mesenchymal stem cells and reverses osteoporosis.

Elabd C, Basillais A, Beaupied H, Breuil V, Wagner N, Scheideler M, Zaragosi LE, Massiéra F, Lemichez E, Trajanoski Z, Carle G, Euller-Ziegler L, Ailhaud G, Benhamou CL, Dani C, Amri EZ.

Source

ISBDC, Université de Nice Sophia-Antipolis, CNRS, Nice, France.

Abstract

Osteoporosis constitutes a major worldwide public health burden characterized by enhanced skeletal fragility. Bone metabolism is the combination of bone resorption by osteoclasts and bone formation by osteoblasts. Whereas increase in bone resorption is considered as the main contributor of bone loss that may lead to osteoporosis, this loss is accompanied by increased bone marrow adiposity. Osteoblasts and adipocytes share the same precursor cell and an inverse relationship exists between the two lineages. Therefore, identifying signaling pathways that stimulate mesenchymal stem cells osteogenesis at the expense of adipogenesis is of major importance for developing new therapeutic treatments. For this purpose, we identified by transcriptomic analysis the oxytocin receptor pathway as a potential regulator of the osteoblast/adipocyte balance of human multipotent adipose-derived stem (hMADS) cells. Both oxytocin (OT) and carbetocin (a stable OT analogue) negatively modulate adipogenesis while promoting osteogenesis in both hMADS cells and human bone marrow mesenchymal stromal cells. Consistent with these observations, ovariectomized (OVX) mice and rats, which become osteoporotic and exhibit disequilibrium of this balance, have significant decreased OT levels compared to sham-operated controls. Subcutaneous OT injection reverses bone loss in OVX mice and reduces marrow adiposity. Clinically, plasma OT levels are significantly lower in postmenopausal women developing osteoporosis than in their healthy counterparts. Taken together, these results suggest that plasma OT levels represent a novel diagnostic marker for osteoporosis and that OT administration holds promise as a potential therapy for this disease.

PMID: 18583541

http://www.ncbi.nlm.nih.gov/pubmed/19369205

Proc Natl Acad Sci U S A. 2009 Apr 28;106(17):7149-54. Epub 2009 Apr 15.

Oxytocin is an anabolic bone hormone.

Tamma R, Colaianni G, Zhu LL, DiBenedetto A, Greco G, Montemurro G, Patano N, Strippoli M, Vergari R, Mancini L, Colucci S, Grano M, Faccio R, Liu X, Li J, Usmani S, Bachar M, Bab I, Nishimori K, Young LJ, Buettner C, Iqbal J, Sun L, Zaidi M, Zallone A.

Source

Department of Human Anatomy and Histology, University of Bari, 70124 Bari, Italy.

Abstract

We report that oxytocin (OT), a primitive neurohypophyseal hormone, hitherto thought solely to modulate lactation and social bonding, is a direct regulator of bone mass. Deletion of OT or the OT receptor (Oxtr) in male or female mice causes osteoporosis resulting from reduced bone formation. Consistent with low bone formation, OT stimulates the differentiation of osteoblasts to a mineralizing phenotype by causing the up-regulation of BMP-2, which in turn controls Schnurri-2 and 3, Osterix, and ATF-4 expression. In contrast, OT has dual effects on the osteoclast. It stimulates osteoclast formation both directly, by activating NF-kappaB and MAP kinase signaling, and indirectly through the up-regulation of RANK-L. On the other hand, OT inhibits bone resorption by mature osteoclasts by triggering cytosolic Ca(2+) release and NO synthesis. Together, the complementary genetic and pharmacologic approaches reveal OT as a novel anabolic regulator of bone mass, with potential implications for osteoporosis therapy.

PMID: 19369205

Free PMC Article

http://www.ncbi.nlm.nih.gov/pubmed/21123938

Clin Calcium. 2010 Dec;20(12):1857-64.

[Control of bone remodeling by nervous system. Possible roles of pituitary hormones for bone metabolism].

[Article in Japanese]

Takeuchi Y.

Source

Toranomon Hospital Endocrine Center, Japan.

Abstract

Accumulating evidence clearly indicates both thyroid hormone and estrogen have a pivotal role in bone metabolism. Pituitary hormones, TSH and FSH, regulate circulating levels of thyroid hormone and estrogen, respectively. Recent works raise a possibility that either TSH or FSH also has its own direct effects on bone cells involved in bone resorption and formation. More recently, it is suggested that oxytocin and vasopressin are also involved in bone metabolism. However, several investigations of genetically manipulated model mice and clinical data from patients with certain diseases have provided inconsistent results. Thus, we need more data that answer the question whether or not each pituitary hormone is physiologically and pathophysiologically involved in controlling bone metabolism in human.

PMID: 21123938

http://en.wikipedia.org/wiki/Semen#Appearance_and_consistency_of_human_semen

Health effects

In addition to its central role in reproduction, some studies have made claims that semen may have certain beneficial effects on human health:

- Antidepressant: One study suggested that vaginal absorption of semen could act as an antidepressant; the study compared two groups of women, one of which used condoms and the other did not.[13][14]
- Cancer prevention: Studies suggested that seminal plasma might reduce breast cancer by "not less than 50 percent."[15][16] This effect is attributed to its glycoprotein and selenium content, with apoptosis being induced by TGF-Beta. A related urban legend parodied these findings and claimed that performing fellatio at least three times a week reduced the risk of breast cancer.[17]
- Preeclampsia prevention: It has been hypothesized that substances in semen condition a mother's immune system to accept the "foreign" proteins found in sperm as well as the resulting fetus and placenta, keeping blood pressure low and thereby reducing the risk of preeclampsia. A study shows that oral sex and swallowing sperm may help make a woman's pregnancy safer and more successful, because she is absorbing her partner's antigens.[18]

Other studies claim adversarial effects:

- Cancer worsening: seminal plasma has prostaglandin elements that could accelerate the development of an already existing cervical cancer.[19]

http://www.ncbi.nlm.nih.gov/pubmed/6146580

Int J Fertil. 1984;29(1):25-32.

Peptide and steroid hormone concentrations in human seminal plasma.

Asch RH, Fernandez EO, Siler-Khodr TM, Pauerstein CJ.

Abstract

Concentrations of peptide (alpha fraction of human chorionic gonadotropin [alpha-hCG], beta fraction of human chorionic gonadotropin [beta-hCG], luteinizing hormone [LH], follicle-stimulating hormone [FSH], and prolactin [PRL]) and steroid hormones (testosterone [T], dihydrotestosterone [DHT], estrone [E1], estradiol [E2] and delta 4-androstenedione [A]) were measured in the seminal plasma of 193 men. They were divided into three groups: group 1--patients attending an infertility clinic; group 2--normal volunteers of proven fertility; and group 3--men vasectomized at least 1 year prior to the study. Correlations among concentrations of hormones in seminal plasma and characteristics of the spermogram were studied. Seminal concentrations of alpha-hCG, beta-hCG, LH, T, and DHT were significantly higher in subjects with sperm in their ejaculate than in vasectomized men. No differences were observed among the groups in seminal concentrations of FSH, PRL, A, E1, and E2. Concentrations of beta-hCG and LH were highly correlated with the numbers and motility of sperm in the ejaculates. Testosterone concentrations were significantly correlated with motility of sperm.

PMID: 6146580

http://www.ncbi.nlm.nih.gov/pubmed/3541686

Andrologia. 1986 Sep-Oct;18(5):470-3.

Calcitonin in human seminal plasma and its localization on human spermatozoa.

Foresta C, Caretto A, Indino M, Betterle C, Scandellari C.

Abstract

We determined the calcitonin (CT) levels in peripheral plasma and in seminal fluid of 15 normal human subjects: the concentration of the hormone in seminal fluid was about 30 times higher than the concentration found in peripheral plasma. We also studied the localization of calcitonin on human spermatozoa by means of an indirect immunofluorescent technique, using an anti-human CT rabbit serum and a fluorescein-isothiocyanate conjugated goat anti-rabbit immunoglobulins serum. A bright fluorescence was observed at the middle piece and neck, while the tail's principal piece was weakly stained. With an anti-human CT rabbit serum pre-absorbed with human CT no fluorescent staining was detectable. These findings demonstrate that calcitonin is localized onto spermatozoa and suggest a potential role for calcitonin in the calcium dependent-mechanisms of spermatozoa.

PMID: 3541686

http://www.sciencedaily.com/releases/2008/10/081031172937.htm

Endocr Rev. 2010 Jun;31(3):266-300. Epub 2010 Jan 5.

From estrogen-centric to aging and oxidative stress: a revised perspective of the pathogenesis of osteoporosis.

Manolagas SC.

Source

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Abstract

Estrogen deficiency has been considered the seminal mechanism of osteoporosis in both women and men, but epidemiological evidence in humans and recent mechanistic studies in rodents indicate that aging and the associated increase in reactive oxygen species (ROS) are the proximal culprits. ROS greatly influence the generation and survival of osteoclasts, osteoblasts, and osteocytes. Moreover, oxidative defense by the FoxO transcription factors is indispensable for skeletal homeostasis at any age. Loss of estrogens or androgens decreases defense against oxidative stress in bone, and this accounts for the increased bone resorption associated with the acute loss of these hormones. ROS-activated FoxOs in early mesenchymal progenitors also divert ss-catenin away from Wnt signaling, leading to decreased osteoblastogenesis. This latter mechanism may be implicated in the pathogenesis of type 1 and 2 diabetes and ROS-mediated adverse effects of diabetes on bone formation. Attenuation of Wnt signaling by the activation of peroxisome proliferator-activated receptor gamma by ligands generated from lipid oxidation also contributes to the age-dependent decrease in bone formation, suggesting a mechanistic explanation for the link between atherosclerosis and osteoporosis. Additionally, increased glucocorticoid production and sensitivity with advancing age decrease skeletal hydration and thereby increase skeletal fragility by attenuating the volume of the bone vasculature and interstitial fluid. This emerging evidence provides a paradigm shift from the "estrogen-centric" account of the pathogenesis of involutional osteoporosis to one in which age-related mechanisms intrinsic to bone and oxidative stress are protagonists and age-related changes in other organs and tissues, such as ovaries, accentuate them.

PMID: 20051526

FULL PAPER http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3365845/?tool=pubmed

http://www.ncbi.nlm.nih.gov/pubmed/12711017

J Steroid Biochem Mol Biol. 2003 Feb;84(2-3):307-16.

The content of four immunomodulatory steroids and major androgens in human semen.

Hampl R, Pohanka M, Hill M, Stárka L.

Source

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Abstract

Seminal fluid fulfils a dual role: it provides optimal conditions for fertilization and protects male germ cells from infections. Besides both major sexual hormones and cortisol it contains a considerable amounts of dehydroepiandrosterone (DHEA), known to counteract the excessive actions of glucocorticoids. From this point of view of importance may be our recent finding of both 7-hydroxy-dehydroepiandrosterone epimers (7-OH-DHEA) in semen, believed to be in some instances the locally active immunoprotective agents. The concentrations of these steroids were of the same range or even higher than in blood. Here further data on 7-OH-DHEA in semen, along with other relevant steroid hormones, are given in 79 samples, either from healthy males or from patients with various sexual disorders. A method has been developed enabling us a simultaneous determination of DHEA, 7-OH-DHEA epimers, testosterone, dihydrotestosterone and cortisol in seminal fluid. It was based on ether extraction, solvent partition and HPLC separation, followed by specific radioimmunoassays in the respective fractions. In addition, the steroids were measured in serum and the concentrations in both fluids were compared. The concentrations of 7-OH-DHEA in seminal fluid varied from 1.8 to 15.7 nmol/l, while those of DHEA were about five times higher.

PMID: 12711017