DOWNLOAD PDF FERTILITY REGULATION TODAY AND TOMORROW (SERONO SYMPOSIA PUBLICATIONS FROM RAVEN PRESS, VOL 36)

Chapter 1 : USA - Controlled release systems and low dose androgens - Google Patents

Fertility Regulation Today and Tomorrow [Serono Symposia Publications from Raven Press, Volume 36] by Diczfalusy, E.; Bygdeman, M., eds.. Raven Press, New York,

Some metabolic and hormonal changes in women using long acting injectable contraceptives. Alexandria Journal of Pharmaceutical Sciences 3 1: Determinants of acceptance of injectable contraception in Bangladesh. The effects of Depo-Provera on carbohydrate, lipids and vitamin metabolism. Journal of Steroid Biochemistry 11 1B: Effects of medroxyyprogessterone acetate on serum lipids, protein, glucose tolerance and liver function in Thai women. A study of the mechanism of weight gain in medroxyprogessterone acetate users Contraception 22 6: Counseling about side effects improves contraceptive continuation. Beagle carcinogenicity studies no longer required for progestogens. Scrip World Pharmaceutical News, No. Acceptability of injectable contraception in the Philippines. An overview of the FPNP injectable programme. Recent advances in contraceptive technology: Proceedings of the seminar held Oct. Monthly injectable contraceptives and breast cancer. Ellis, Ellis Pharmaceutical Consulting, May 31, Risk of human immunodeficiency virus and Hepatitis-B virus transmission through unsafe injections: A new class of potent progestins. Journal of the American Chemical Society 80 pt. Analyse situationnelle du programme de planification familiale au Burkina Faso. Burkina Faso, Burkina Faso. Department of Health, Feb. Studies in Family Planning 9 Return of fertility following discontinuation of an injectable contraceptie-Norethisterone oenanthate NET EN mg dose. Bangladesh Demographic and Health Survey A study of women who conceived after discontinuation of Depo Provera. A study of Depo-Provera users in a family planning clinic in Sri Lanka. Review of ovulation return upon discontinuation of once-a-month injectable contraceptives. A comparative study on the return to ovulation following chronic use of once-a-month injectable contraceptives. Determinants of menstrual bleeding patterns among women using natural and hormonal methods of contraception: The influence of individual characteristics. The analysis of menstrual bleeding patterns: The analysis of vaginal bleeding patterns by fertility regulating methods. The association between vaginal bleeding patterns and reasons for discontinuation of contraceptive use. Depo medroxyprogesterone acetate Depo Provera for contraception. Benson and Pernolls handbook of obstetrics and gynecology. New York, McGraw-Hill, Improving contraceptive supply management. Family Planning Manager 1 4: Depot medroxyprogesterone acetate Depo-Provera as a contraceptive preparation. South African Medical Journal 45 Oral contraception and congenital malformations in offspring: Obstetrics and Gynecology 76 3,Pt. Acceptability of Depo-Provera as a reliable contraceptive method. Amsterdam, Excerpta Medical Foundation, International Congress Series No. Contraceptive use and breast-feeding duration in rural Bangladesh. European Journal of Clinical Nutrition 45 7: Anaphylactoid shock with medroxyprogesterone acetate: Journal of the Louisiana State Medical Society Short term increase in risk of breast cancer after full term pregnancy. British Medical Journal What does the Metlab fertility experience and really show? National Centre for Epidemiology and Population Health, Health Transition Working Paper No. Alterations in blood sugar, protein, and lipid levels in Indian women by norethisterone enanthate. International Journal of Fertility 32 3: Proceedings of the symposium Progesterone, progestins, and fetal development. Fertility and Sterility 30 1: New regimen of injectable contraceptives. Journal of the Medical Association of Thailand 70 4: Concentration of fat, protein, lactose and enery in milk of mothers using hormonal contraceptives. Annals of Tropical Paediatrics 12 2: Manila Bulletin, May 1, A prospective study of adolescents who choose among levonorgestrel implant Norplant , medroxyprogesterone acetate Depo-Provera , or the combined oral contraceptive pill as contraception. Fertility regulation today and tomorrow. New York, Raven, Serono Symposia Publications Vol. Recovery of bone density in women who stop using medroxyprogesterone acetate. Bone density in women receiving depot medroxyprogesterone acetate for contraception. A changing pattern in the association of oral contraceptive and the different groups of congenital limb deficiencies. Some

effects of depo-medroxyprogesterone acetate DMPA: Observations in the nursing infant and in the long-term user. International Journal of Gynaecology and Obstetrics 20 1: Vaginal bleeding patterns of women using different contraceptive methods Implants, injectables, IUDs, oral pills An Indian experience. Geburtshilfe und frauenheilkunde 17 Medroxyprogesterone acetate and homozygous sickle-cell disease. Quality of care in family planning in Latin America. Advances in Contraception 9 2: Diseases of the breast. Depo-provera medroxyprogesterone acetate for contraception: A current perspective of scientific, clinical and social issues. Proceedings of an international symposium held on Nov. Oxford, England, Oxford Clinical Communications, A partnership for urban health and family planning in Bangladesh. An assessment of programme needs in zone 3 of Dhaka City. Ministry of Health and Family Welfare. Long-term use of depot medroxy progesterone acetate as a contraceptive. Acta Obstetricia et Gynecologica Scandinavica Egypt Demographic and Health Survey A prospective, one-year study on the effects of two long acting injectable contraceptives depot-medroxyprogesterone acetate and norethisterone oenanthate on serum and lipoprotein lipids. Hormone and Metabolic Research 24 2: Effect of long-acting progestagen-only injectable contraceptives on carbohydrate metabolism and its hormonal profile. Effect of depo-medroxyprogesterone acetate on coagulation factors and serum lipids in Egyptian women. Alterations in blood lipids and side effects induced by Depo-Provera in Nigerian women. The effects of depo-provera on serum protein levels in Nigerian women. Journal of Steroid Biochemistry 20 2: Experience with the use of depo-medroxyprogesterone acetate in a Nigerian population. African Journal of Medicine and Medical Sciences 17 4:

Chapter 2 : Zubal Books Complete Catalog Page 31

Note: Citations are based on reference standards. However, formatting rules can vary widely between applications and fields of interest or study. The specific requirements or preferences of your reviewing publisher, classroom teacher, institution or organization should be applied.

Sustained release formulations substantially free of organic solvent, and sustained release formulations for maintaining low serum levels of androgen are disclosed. Novel sustained release formulations and methods for their production and use are disclosed. Some preferred embodiments to novel formulations of injectable forms of medroxyprogesterone acetate and megestrol acetate which yield predetermined circulating levels of active ingredients for prolonged periods of time. Biodegradable microparticles are provided which release, for example, medroxyprogesterone acetate and megestrol acetate, at a near constant and slow rate when injected to warm-blooded animals including the human for the prevention and treatment of diseases as well as fertility control. Novel methods for removing undesirable residual solvent from sustained release particles are also provided. The role of estrogens in promoting the growth of estrogen-sensitive breast cancer is well recognized Lippman, Semin. Chronic exposure to estrogens unopposed by progesterone can lead to the development of endometrial hyperplasia which predisposes to endometrial carcinoma Lucas, Obstet. The incidence of endometrial cancer increases after menopause, especially in women receiving estrogen therapy without simultaneous treatment with progestins Smith et al. A known form of endocrine therapy in premenopausal women is castration most commonly performed by surgery or irradiation, two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists LHRH agonists which, following inhibition of secretion of bioactive Luteinizing Hormone LH by the pituitary gland, decrease serum estrogens to castrated levels Nicholson et al. Beneficial effects of treatment with LHRH agonists have also been observed in postmenopausal women Nicholson et al. Various LHRH agonists and antiandrogens are discussed. Antiandrogens, antiestrogens, certain inhibitors of sex steroid biosynthesis and blocking of hormonal output are discussed. Press, New York, , pp. Androgen receptors are also present in dimethylbenz a anthracene DMBA -induced mammary tumors in the rat Asselin et al. The growth inhibitory effects of the androgen methyltrienolone R , on endometrial carcinoma in vitro have been described Centola, Cancer Res. Many studies subsequently confirmed the beneficial effect of androgens on breast cancer Alan and Herrman, Ann. These initial results stimulated cooperative studies on the effect of testosterone propionate and DES which were both found to be effective in producing objective remissions. The median duration of survival was four times longer in the responders as compared to the non-responder group 27 versus 7. Of these women, 17 had also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to Tamoxifen and in those who had failed. Of the 17 patients who had failed to both Tamoxifen and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either Tamoxifen or hypophysectomy. There was a tendency for improved survival in the combination therapy arm versus days. Moreover, patients treated with Tamoxifen and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen Torney et al. As mentioned above, Poulin et al. The inhibitory effect of androgens on the growth of human breast carcinoma cells ZR has also been observed in vivo in nude mice Dauvois and Labrie, Cancer Res. Similar inhibitory effects were observed on the levels of ER mRNA measured by ribonuclease protection assay. Such data on estrogen receptor expression provide an explanation for at least part of the antiestrogenic effects of androgens on breast cancer cell growth and moreover suggest that the specific inhibitory effects of androgen therapy could be additive to the standard treatment limited to blockade of estrogens by antiestrogens. That DHT acts through interaction with the androgen receptor is supported by the finding that simultaneous treatment with the antiandrogen Flutamide completely prevented DHT action. Particularly illustrative of the potent inhibitory

effect of the androgen DHT on tumor growth are the decrease by DHT of the number of progressing tumors from The number of new tumors appearing during the day observation period in estradiol-treated animals decreased from 1. Such data demostrate, for the first time, that androgens are potent inhibitors of DMBA-induced mammary carcinoma growth by an action independent from inhibition of gonadotropin secretion and suggest an action exerted directly at the tumor level, thus further supporting the in vitro data obtained with human ZR breast cancer cells Poulin et al. Its more general use, however, is for breast cancer relapsing after other endocrine therapeutic modalities. The maximal inhibitory action of medroxyprogesterone acetate MPA on human breast cancer cell growth in vitro may be achieved at concentration as low as 1 nM while an approximately fold higher dose is often required for glucocorticoid action Poulin et al. This steroid, however, presents a high affinity for progesterone PgR as well as for androgen AR and glucocorticoid receptors GR in various animal tissues Perez-Palacios et al. It is known that in addition to progesterone receptors PgR , most synthetic progestational agents bind with significant affinity to androgen AR as well as glucocorticoid GR receptors, and induce biological actions specifically determined by these individual receptor systems Labrie et al. Mechanisms of Steroid Action G. Grisburg, eds , MacMiland Press, London, pp. Accordingly, several side effects other than progestational have been noted in patients treated with MPA. Despite its high affinity for AR, MPA seldom causes significant virilizing symptoms acne, hirsutism, etc. Haller and Glick, Semin. Suppression of adrenal function by MPA is believed to be caused both by an inhibitory action on ACTH secretion at the pituitary level and by direct inhibition of steroidogenesis at the adrenal level Blossey et al. Moreover, its inhibitory effect on gonadotropin secretion is clearly exerted through its direct interaction with pituitary AR in the rat Labrie et al. Other synthetic progestins have also been shown to possess, in addition to their progesterone-like activity, various degrees of androgenic activity Labrie et al. The androgen methyltesiosterone has been shown to relieve the symptoms of endometriosis Hamblen, South Med. Androgenic and masculinizing side effects sometimes irreversible are however important with potent androgenic compounds such as testosterone and its derivatives. High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been successfully used for the treatment of endometrial cancer Tatman et al. High dose MPA is being used with a success similar to that of Tamoxifen for the treatment of endometrial carcinoma Rendina et al. Androgenic and masculinizing side effects sometimes irreversible are however important with potent androgenic compounds such as testosterone. Orchiectomy in rats can cause osteoporosis detectable within 2 months Winks and Felts, Calcif. Moreover, elevated androgens in postmenopausal women have been shown to protect against accelerated bone loss Deutsch et al. In agreement with such a role of androgens, urinary levels of androgen metabolites are lower in postmenopausal symptomatic menopausis than in matched controls and a significant decrease in conjugated dehydroepiandrosterone DHEA was found in the plasma of osteoporotic patients Hollo and Feher, Acta Med. It has even been suggested that postmenopausal osteoporosis results from both hypoestrogenism and hypoandrogenism Hollo et al. A significant bone loss is seen in men at about 80 years of age, with the accompanying occurrence of hip, spine and wrist fractures. Several studies indicate that osteoporosis is a clinical manifestation of androgen deficiency in men Baran et al. In fact, androgen deficiency is a major risk for spinal compression in men Seeman et al. Decreased radial and spinal bone density accompanies hypogonadism associated with hyperprolactinernia Greespan et al. However, in these cases, the role of hyperprolactinemia and loss in body weight is uncertain. Bone density is in fact reduced in both primary and secondary hypogonadism Velentzas and Karras. In addition, serum calcitonin has been found to be reduced in hypogonadal men Foresta et al. Androgens have also been shown to increase osteoid synthesis and mineralization in chicken Puche and Rosmano, Calif. Androgen therapy in hypogonadal men increases skeletal growth and maturation Webster and Hogkins, Proc. In addition, testosterone therapy in man has been shown to cause positive nitrogen, calcium and phosphate balance Albright, F. The parathyroid glands and metabolic bone disease. Williams and Williams Co.: As studied by bone histomorphometry, testosterone therapy in hypogonadal males resulted in increases in relative osteoid volume, total osteoid surface, linear

extend of bone formation and bone mineralization Barau et al. There was also a decrease in plasma phosphate probably due to an effect on renal tubular reabsorption of phosphates Selby et al. Testosterone therapy increases bone formation in men with primary hypogonadism Baron et al. In men with already fused epiphyses, however, there was a significant increase in cortical bone density while no significant change was observed on trabecular bone density, thus supporting previous suggestions of variable sensitivity of cortical and trabecular bone to steroid therapy. More recently, using total body calcium measurements by neutron activation as parameter, the anabolic steroid methandrostenolone has shown positive and relatively long-term months effects in a double-blind study in postmenopausal osteoporosis Chessnut et al. Such data confirm experimental data in rabbits and dogs when nandrolone decanoate reduced bone resorption Ohem et al. Moreover, in osteoporotic women Dequeker and Geusens, Acta Endocrinol. Vitamin D treatment, on the other hand, only reduced bone resorption. Such data are of interest since while most therapies are limited to an arrest of bone loss, an increased in bone mass was found with the use of the anabolic steroid nandrolone. A similar stimulation of bone formation by androgens has been suggested in a hypogonadal male Baran et al. The problem with regimens which inhibit bone resorption with calcium, calcitriol or hormones is that they almost certainly lead to suppression of bone formation Need et al. Anabolic steroids, compounds having fewer virilizing effects, were subsequently developed. Although, minimal effects have been reported by some Wilson and Griffin, Metabolism A randomized study in postmenopausal women has been shown an increase in total bone mass during treatment with the anabolic steroid stanazolol although side effects were recorded in the majority of patients Chessnut et al. Such progestins have, at times, been synthesized with the aim of developing compounds acting as analogs of progesterone on the progesterone receptors, especially for the control of fertility. With the availability of new and more precise tests, however, it became evident that such compounds, originally made to interact exclusively with the progesterone receptor, do also interact, frequently with high affinity, with the androgen receptor Labrie et al. Sometimes, the androgenic activity of these compounds, especially at low concentrations, becomes more important than the true progestin activity. This is the case, for example, for medroxyprogesterone acetate Poulin et al. The blockade of estrogens, another common treatment for breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for endometriosis, has similar undesirble deleterious effects on bone mass in women. This include steroids with intrinsic long action after injection e. Depoprovera; or more recently, through the use of extrinsic delivery systems, e. In addition, it is estimated that 0. Contraceptive preparations which allow protection over extended periods of time have been developped over the last 25 years. More than 10, women-month were studied in each group. Late for injection, personal reasons and lost to follow-up amounted to Such data indicate the need for more easily acceptable schedules of administration. In a smaller study women-month , DepoMPA, at the same dose, led to a discontinuation rate of Oral administration is limited by problems of compliance and fluctuating blood levels while release of MPA from Depoprovera injection is rapid at first and declines in a highly variable fashion at later time intervals. Similar arguments apply to MGA. See, for example and references, R. Scribner disclose the use a polylactide-drug mixtures, especially steroids such as medroxyprogesterone acetate, for slow sustained release of the drugs. Leonard discloses fused recrystallised steroid drug pellet useful as sustained release implant.

Chapter 3 : :: Asian Journal of Andrology ::

In: Fertility regulation today and tomorrow, [edited by] E. Diczfalusy and M. Bygdeman. New York, New York, Raven Press, (Serono Symposia Publications from Raven Press, Volume 36).

What is claimed is: A method of treating or preventing osteoporosis by administering to a patient in need of such treatment or prevention, an effective amount of sustained release particles, with or without additional pharmaceutical carrier or diluent, said particles comprising an androgenic steroid selected from the group consisting of medroxyprogesterone acetate or megestrol acetate, wherein said androgenic steroid is dispersed within a sustained-release binder which is biocompatible with human tissue and which undergoes biodegradation in the body into biocompatible metabolic products, wherein said particles are capable, under standard conditions, of releasing said androgenic steroid during and as result of said biodegradation of said binder at a rate and duration which maintains circulating serum levels of said androgenic steroid between 1. FIELD OF THE INVENTION This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating endometriosis in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients to be used in the therapy. Novel sustained release formulations and methods for their production and use are disclosed. Some preferred embodiments to novel formulations of injectable forms of medroxyprogesterone acetate and megestrol acetate which yield predetermined circulating levels of active ingredients for prolonged periods of time. Biodegradable microparticles are provided which release, for example, medroxyprogesterone acetate and megestrol acetate, at a near constant and slow rate when injected to warm-blooded animals including the human for the prevention and treatment of diseases as well as fertility control. Novel methods for removing undesirable residual solvent from sustained release particles are also provided. The role of estrogens in promoting the growth of estrogen-sensitive breast cancer is well recognized Lippman, Semin. Estrogens are also known to promote the proliferation of normal endometrium. Chronic exposure to estrogens unopposed by progesterone can lead to the development of endometrial hyperplasia which predisposes to endometrial carcinoma Lucas, Obstet. The incidence of endometrial cancer increases after menopause, especially in women receiving estrogen therapy without simultaneous treatment with progestins Smith et al. Various investigators have been studying hormone-dependent breast and endometrial cancer. A known form of endocrine therapy in premenopausal women is castration most commonly performed by surgery or irradiation, two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists LHRH agonists which, following inhibition of secretion of bioactive Luteinizing Hormone LH by the pituitary gland, decrease serum estrogens to castrated levels Nicholson et al. Several studies show that treatment of premenopausal breast cancer patients with LHRH agonists induces responses comparable to those achieved with other forms of castration Klijn et al. Beneficial effects of treatment with LHRN agonists have also been observed in postmenopausal women Nicholson et al. Various LHRH agonists and antiandrogens are discussed. WIPO International Publication WO discuss certain 16,16 disubstituted androstene steroid compounds for hair growth and skin disorders. Antiandrogens, antiestrogens, certain inhibitors of sex steroid biosynthesis and blocking of hormonal output are discussed. Androgen receptors have been shown to be present in normal Witliff, In: Press, New York, , pp. Androgen receptors are also present in dimethylbenz a anthracene DMBA -induced mammary tumors in the rat Asselin et al. Androgen receptors have also been described in human endometrium MacLaughlin and Richardson, J. The growth inhibitory effects of the androgen methyltrienolone R , on endometrial carcinoma in vitro have been described Centola, Cancer Res. Recent reports have indicated that androgen receptors may add to the selective power of estrogen receptors or even supplant estrogen receptors as best predicting response to endocrine therapy Teulings et al. The first androgen successfully used in the treatment of advanced breast cancer is testosterone propionate Nathanson, Rec. Many studies

subsequently confirmed the beneficial effect of androgens on breast cancer Alan and Herrman, Ann. These initial results stimulated cooperative studies on the effect of testosterone propionate and DES which were both found to be effective in producing objective remissions. The median duration of survival was four times longer in the responders as compared to the non-responder group 27 versus 7. Of these women, 17 had also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to Tamoxifen and in those who had failed. Of the 17 patients who had failed to both Tamoxifen and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either Tamoxifen or hypophysectomy. The combination Fluoxymesterone and Tamoxifen has been shown to be superior to Tamoxifen alone. There was a tendency for improved survival in the combination therapy arm versus days. The independent beneficial effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to Tamoxifen could respond to Fluoxymesterone and vice versa. Moreover, patients treated with Tamoxifen and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen Tormey et al. Since testosterone propionate had beneficial effects in both pre- and post-menopausal women Adair et al. Recent in vitro studies describe the relative antiproliferative activities of an androgen on the growth of the estrogen-sensitive human mammary carcinoma cell line ZR Poulin et al. As mentioned above, Poulin et al. The inhibitory effect of androgens on the growth of human breast carcinoma cells ZR has also been observed in vivo in nude mice Dauvois and Labrie, Cancer Res. As a possible mechanism of androgen action in breast cancer, it has recently been shown that androgens strongly suppress estrogen ER and progesterone PgR receptor contents in ZR human breast cancer cells as measured by radioligand binding and anti-ER monoclonal antibodies. Similar inhibitory effects were observed on the levels of ER mRNA measured by ribonuclease protection assay. Such data on estrogen receptor expression provide an explanation for at least part of the antiestrogenic effects of androgens on breast cancer cell growth and moreover suggest that the specific inhibitory effects of androgen therapy could be additive to the standard treatment limited to blockade of estrogens by antiestrogens. That DHT acts through interaction with the androgen receptor is supported by the finding that simultaneous treatment with the antiandrogen Flutamide completely prevented DHT action. Particularly illustrative of the potent inhibitory effect of the androgen DHT on tumor growth are the decrease by DHT of the number of progressing tumors from The number of new tumors appearing during the day observation period in E2 -treated animals decreased from 1. Such data demonstrate, for the first time, that androgens are potent inhibitors of DMBA-induced mammary carcinoma growth by an action independent from inhibition of gonadotropin secretion and suggest an action exerted directly at the tumor level, thus further supporting the in vitro data obtained with human ZR breast cancer cells Poulin et al. Since the natural androgens TESTO and DHT have strong masculinizing effects, numerous derivatives of TESTO as well as progesterone have been synthesized in order to obtain useful compounds having fewer undesirable masculinizing side effects body hair growth, loss of scalp hair, acne, seborrhea and loud voice. Medroxyprogesterone acetate MPA is one of the most widely used compounds in the endocrine therapy of advanced breast cancer in women Mattsson, Breast Cancer Res. Its more general use, however, is for breast cancer relapsing after other endocrine therapeutic modalities. The maximal inhibitory action of medroxyprogesterone acetate MPA on human breast cancer cell growth in vitro may be achieved at concentration as low as 1 nM while an approximately fold higher dose is often required for glucocorticoid action Poulin et al. Until recently, the mechanisms underlying the antitumor activity of MPA were poorly understood and have been attributed to interaction with the progesterone receptor. This steroid, however, presents a high affinity for progesterone PgR as well as for androgen AR and glucocorticoid receptors GR in various animal tissues Perez-Palacios et al. It is known that in addition to progesterone receptors PgR , most synthetic progestational agents bind with significant affinity to androgen AR as well as glucocorticoid GR receptors, and induce biological actions specifically determined by these individual receptor systems Labrie et al. Mechanisms of Steroid Action G. Grisburg, eds , MacMiland Press, London, pp. Accordingly, several side

effects other than progestational have been noted in patients treated with MPA. The inhibitory effect of MPA on gonadotropin secretion is clearly exerted through its direct interaction with pituitary AR in the rat Labrie et al. Despite its high affinity for AR, MPA seldom causes significant virilizing symptoms ache, hirsutism, etc. Haller and Click, Semin. The most easily explained adverse side effects of MPA are related to its glucocorticoid-like action with Cushingoid syndrome, euphoria and subjective pain relief Mattsson, Breast Cancer Res. Suppression of adrenal function by MPA is believed to be caused both by an inhibitory action on ACTH secretion at the pituitary level and by direct inhibition of steroidogenesis at the adrenal level Blossey et al. Haller and Glick, Semin. Moreover, its inhibitory effect on gonadotropin secretion is clearly exerted through its direct interaction with pituitary AR in the rat Labrie et al. Other synthetic progestins have also been shown to possess, in addition to their progesterone-like activity, various degrees of androgenic activity Labrie et al. High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been successfully used for the treatment of endometrial cancer Tatman et al. The androgen methyltestosterone has been shown to relieve the symptoms of endometriosis Hamblen, South Med. Androgenic and masculinizing side effects sometimes irreversible are however important with potent androgenic compounds such as testosterone and its derivatives. High dose MPA is being used with a success similar to that of Tamoxifen for the treatment of endometrial carcinoma Rendina et al. Androgenic and masculinizing side effects sometimes irreversible are however important with potent androgenic compounds such as testosterone. In analogy with the androgen-induced decrease in estrogen receptors in human breast cancer ZR cells Poulin et al. Studies in animals have shown that androgen deficiency leads to osteopenia while testosterone administration increases the overall quantity of bone Silberberg and Silberberg, ; see Finkelstein et al. Orchiectomy in rats can cause osteoporosis detectable within 2 months Winks and Felts, Calcif. While hirsute oligomenorrheic and amenorrheic women having low circulating E2 levels would be expected to have reduced bone mass, these women with high androgen but low estrogen levels are at reduced risk of developing osteoporosis Dixon et al. Adrenal androgen levels have been found to be reduced in osteoporosis Nordin et al. Moreover, elevated androgens in postmenopausal women have been shown to protect against accelerated bone loss Deutsch et al. In agreement with such a role of androgens, urinary levels of androgen metabolites are lower in postmenopausal symptomatic menopausis than in matched controls and a significant decrease in conjugated dehydroepiandrosterone DHEA was found in the plasma of osteoporotic patients Hollo and Feher, Acta Med. It has even been suggested that postmenopausal osteoporosis results from both hypoestrogenism and hypoandrogenism Hollo et al. As a mechanism for the above-suggested role of both estrogens and androgens in osteoporosis, the presence of estrogen Komm et al. In boys, during normal puberty, an increase in serum testosterone levels procedes an increase in alkaline phosphate activity marker of osteoblastic activity which itself precedes increased bone density Krabbe et al. While, in women, there is a rapid bone loss starting at menopause, bone loss in males can be recognized at about 65 years of age Riggs et al. A significant bone loss is seen in men at about 80 years of age, with the accompanying occurrence of hip, spine and wrist fractures. Several studies indicate that osteoporosis is a clinical manifestation of androgen deficiency in men Baran et al. Although less frequent than in women osteoporosis can cause significant morbidity in men Seeman et al. In fact, androgen deficiency is a major risk for spinal compression in men Seeman et al. Decreased radial and spinal bone density accompanies hypogonadism associated with hyperprolactinemia Greespan et al. However, in these cases, the role of hyperprolactinemia and loss in body weight is uncertain. Hypogonadism in the male is a well-recognized cause of osteoporotic fracture Albright and Reinfenstein, ; Saville, Clin. Bone density is in fact reduced in both primary and secondary hypogonadism Velentzas and Karras. Severe osteopenia as revealed by decreased cortical and trabecular bone density was reported in 23 hypogonadotropic hypogonadal men Finkelstein et al. Androgenic-reversible decreased sensitivity to calcitonin has been described in rats after castration Ogata et al. In addition, serum calcitonin has been found to be reduced in hypogonadal men Foresta et al. Albright and Ruferstein originally suggested that androgens increase the synthesis of bone matrix. Androgens have also been shown to increase osteoid synthesis and

mineralization in chicken Puche and Rosmano, Calif. Androgen therapy in hypogonadal men increases skeletal growth and maturation Webster and Hogkins, Proc. In addition, testosterone therapy in man has been shown to cause positive nitrogen, calcium and phosphate balance Albright, F. The parathyroid glands and metabolic bone disease. Williams and Williams Co.:

Chapter 4 : The potential and limitations of epidemiological studies. | calendrierdelascience.com

Fertility Regulation Today and Tomorrow (Serono Symposia Publications From Raven Press, Vol 36), edited by E. Diczfalusy and M. Bygdeman, pp, with illus, $49, New York, Raven Press, Back Trouble: A New Approach to Prevention and Recovery, by Deborah Caplan, pp, with illus, $, Gainesville, Florida, Triad Publishing Company,

Experience in Latin America S. Mesigyna, once-a-month injectable contracep- terone enanthate and 5 mg estradiol valerate. The preg- tive, menstrual bleeding. The overall discontin- uation rate at one year was Discontinuation rate for Introduction I bleeding problems was 5. The Colombian women had mmediately after the widespread introduction of a significant increase p ,0. The discontinuation rate for tries, it became evident that alternative steroid amenorrhea was 1. There were no significant differ- hormone delivery systems to eliminate daily pill- taking, particularly in some cultural settings in the ences between the groups regarding discontinuation for less developed world, were needed to facilitate their other medical or non-medical reasons. Mean weight gain administration. Thus originated development of re- after one year of use was 1. Mesigyna is an appropiate search needed for long-acting contraception. Most of once-a-month injectable contraceptive for Latin American the worldwide research efforts carried out in this women since it is highly effective and its perception of direction during the past 25 years have been focused normal menstrual bleeding is of importance in the Latin on developing sustained-release formulations of ste- roids to be used either as injectable contraceptives ICs or as subdermal contraceptive implants. Mexico make the hypodermic injection an ideal method of Name and address for correspondence: The endometrial bleed- Coahuila, Mexico. Number of subjects by country stimulated large research programs aimed at improv- Country Subjects ing the currently available injectables formulations. It developed a strategy for the devel- opment of once-a-month contraceptives which in- volved developing a product containing norethi- pertension, recent or severe liver disease, diagnosed or sterone oenanthate and oestradiol valerate. American countries regarding cycle control, side ef- The initial assessment of each subject was under- fects, and contraceptive efficacy of Mesigyna, a once taken on day 23â€”25 of the cycle prior to admission a-month combined injectable 50 mg noresthisterone into the study. Women had a screening interview and enanthate and 5 mg estradiol valerate. Those subjects who fulfilled the criteria were asked to return to the Materials and Methods clinic on day 1â€”5 of their next menstrual cycle. At Preparation this time they were admitted into the study, and Mesigyna, 50 mg norethisterone enanthate 17a-ethi- given the first injection. Subsequent injections were nylestrenoneheptanoate and 5 mg estradiol given at 30 6 3 days intervals for a total of 12 valerate, was manufactured and formulated in an oily injections. Subjects were followed-up monthly up to solution by Schering AG, Berlin. It was injected as a 1 one year. Every month, the women had a complete mL solution. Menstrual diary cards were given to all women Study Design participating in the study at the time of screening, All subjects were normal, healthy women between 18 and kept by the women during the entire study and 35 years old. They were not pregnant or lactating, period. Subjects were asked to complete their diary on and had regular menstrual cycles for 6 months prior a daily basis. At each follow-up visit, complaints to admission to the study. If a Both postpartum and postabortion women were woman wished to terminate method use for any required to have had regular cycles for 6 months prior reason or was advised to do so by the physician to pregnancy, and to have experienced one normal responsible for the study, a full physical examination cycle since delivery or abortion. The women consented voluntarily to participate in The clinical trial was conducted in six Latin Amer- the trial and were free to refuse a subsequent injection ican countries; Argentina, Ecuador, Colombia, Brazil, at any time during the study. All subjects were Peru, and Mexico, and coordinated by Strategy Center willing to rely solely on this treatment as a method of Canada-Latin America. Exclusion criteria for recruitment were: Ta- vaginal bleeding of unknown etiology, confirmed hy- ble 1 shows the number of eligible subjects recruited Contraception Mesigyna Experience ; No changes in Papanicolaou smear grade the clinical centeres in each country. The total cycles were reported. Non-medical reasons for dis- regard to age

overall mean 6 SD, There were no significant differences year in the study. Weight Change There was weight gain between admission and 3, 6, 9, Contraceptive Efficacy and 12 months follow-up visits. The mean weight The study subjects were analyzed after a follow up of gain was 0. The pregnancy rate was zero pregnancy Only four women discontinued method use giving per users at the end of contraceptive use. The mean change in body weight for these four women during the study period was 5 kg. The number of women who completed the study, discontinued method use or were lost to Blood Pressure follow-up is shown by group in Table 2. The cumulative life table discontinuation rates for 6, 9, and 12 months follow-up visits were The mean changes uation rates at one year for each discontinuation of DBP at 3, 6, 9, and 12 months were As expected in any multi- One One subject had a measurement above the defined country, Argentina, reported a substantially lower limits for hypertension SBP. The 1-year cumultive discontinuation rates for all reasons, excluding study termination, were 7. The remaining complaints were miscel- The overall rate of amenorrhea in all the countries laneous. The percentage of women with new com- was low. The cumulative discontinuation rate for plaints decreased steadily at each follow-up visit for amenorrhea at one year was 1. In all, 23 women discontin- the percentage of women complaining of headaches ued for other medical reasons. Of these women, four between the first and second scheduled follow-up discontinued due to weight gain, seven because of visit. The percentage of women with such a com- headaches, one due to hypertension. The remaining women and continued to drop during the course of the study. None of the women reported study. The mean cycle duration was An average of two women per country had ages of subjects who had headache and in those who amenorrhea, nine subjects had dysmenorrhea, and had any complaints at the first and sixth month five subjects had irregular bleeding. The proportion of women having no complaints gradually increased over the study period for all Discussion countries. In addition to headache, breast tenderness, This multicentered clinical trial provided a total of bleeding problems and dysmenorrhea, there were a woman-months of experience to evaluate the variety of complaints such as decreased libido, acne, once-a-month injectable contraceptive regimen in the nervousness and sleeplessness, which could not be Latin American population. These other complaints were slight and subsided confirmed that in Latin American women Mesigyna with continuous use of the injectable contraceptive. Overall discontinuation rate at 1 year for Vaginal Bleeding Analysis pregnancy was zero per woman-years for a total Completed menstrual dairy cards were obtained from experience of woman-months. This high contra- all subjects throughout the study. Cumulative life table discontinuation rate at one year by reason and country Countries Amenorrhea Bleeding problems Other medical reason Lost to follow-up All reasons AR 0. Percentage of subjects with complaint at the first a pregnancy rate of 0. The present study showed that the one-year EC 6. There were significant BR 1 1. Mesigyna BR 0 0 0 PE 0 1. For amenorrhoea, the discontinuation EC 0 0 0 rate at one year was 1. It should be 1. International Federation of Family Planning. Injectable stressed that this is an analysis of reasons for discon- contraception declaration. Contraceptive failure, method related discontinuation and resumption of use: There- from the National Survey of Family Growth. Fam fore, cultural attitudes and the relation between the Plann Perspect ; The politics of contraception, Vols 1 and 2. Stanford Alumni Association, Patterns of bleeding associated with the use There was little change of mean weight over the 1 of steroid contraceptives. Endometrial Bleeding and Steroidal year of study, similar to the Chinese study. Facts about injectable con- blood pressure and blood pressure change necessi- traceptives: Bull tated treatment discontinuation in only one case. Dicz- significant drop-out rate. The discontinuations due to falusy E, Bygdeman M, eds. Fertility Regulation Today and Tomorrow. Serono Symposia Publica- bleeding problem were significantly higher in the tions, Raven Press, ; World Health Organization, Special Programme of Re- As reported in previous studies,7,8,10,11 more than search, Development and Research Training in Human three-quarters of the women reported no complaint Reproduction. There were no significant arations given once-a-month by intramuscular injec- tion. Contraceptive efficacy and side effects. Contra- differences in discontinuation rates for other medical ception , The bleeding pattern results are similar to other search, Development and Research Training in Human studies. Task Force on Long-acting Systemic trol and more acceptable bleeding patterns

than other Agents for Fertility Regulation. A multicentred phase monthly injectables contraceptives. III comparative study of two hormonal contraceptive preparations given once-a-month by intramuscular in- The present study provides convincing clinical re- jection. The comparison of bleeding patterns. Con- sults which demostrate that Mesigyna is highly effec- traception ; Contraception month injectable contraceptive for Latin American ; Once-a-month regimens and depot-medroxyprogesterone acetate. Fi- combined injectable contraceptives. J Obstet Gynecol nal Report. Task Force on Long-acting Systemic duration of three years.

Chapter 5 : Results for M-Bygdeman | Book Depository

In: Diczfalusy E and Bygdeman M (Eds) Fertility Regulation Today and Tomorrow. Serono Symposia Publications, Vol 36, Raven Press, New York, pp Google Scholar

The only effective technique available for male contraception is vasectomy, being practiced world wide, despite that it is a permanent surgical procedure and its successful reversal is not assured. The drug is currently under multicentre Phase III clinical trial. However, a number of clinical trials substantiate a view that it is indeed possible to have a male contraceptive that meets all the essential criteria in the near future[]. The present review summarizes the advantages and disadvantages of the issues related to various vas-based methods of contraception. It is safe, with minimal morbidity and almost no mortality, effective and simple as a one step procedure. In the past three decades, it has been practiced in over 40 million couples world wide[9]. Contraindications to vasectomy include scrotal pathology, haematoma, allergy to local anaesthesia, genito-urinary or groin infections and sperm granulomas[10,11]. Fear of cardiovascular sequelae and an increased risk of prostate and testicular cancer have also been indicated[6]. A WHO consultation reviewed the available evidences and reported that any casual relationship between vasectomy and the risk of cancer of the prostate or testis is unlikely and that in the existing family planning polices of WHO towards vasectomy, no changes are warranted[12]. In Denmark, over 73, vasectomized men were identified and registered between and without indication of increased risk of testicular cancer due to vasectomy[17]. Hence further investigations are warranted and being pursued. In India, the technique was acceptable to more educated and higher income men and the number of vasectomy acceptances increased three times as compared to the conventional counterpart during the corresponding period[22,23]. However, similar to conventional vasectomy, this method also does not assure a successful reversal. Sperm passage was inhibited temporarily and the luminal patency of the vas could be restored by removing the intravasal thread IVT [25]. As long as the IVT remained in place in the vas, sperm passage was successfully inhibited. When the IVT was removed , the patency of the vas lumen was restored. Histological studies showed no tissue reaction in the vas. The prevention of sperm passage is believed to be due to mechanical obstruction by the IVT[27,28]. This study laid a foundation for a variety of other occlusive techniques that followed. However, there was no guarantee of absolute sterility[29]. PROPLAST, an intravasal plastic device, in the vas of pigs showed appearance of motile spermatozoa throughout the period of observation in serial sperm analysis[30]. Removal of the device restored sperm passage in 2 weeks[31]. No inflammation and other abnormalities were reported. To deliver an electric current, an external battery or a miniature battery inside the body has been tried [36]. The miniature battery, on the other hand, was impractical as the energy storage was very small. The battery becomes drained in a short time necessitating frequent surgical manipulations. As an alternative approach, a biogalvanic cell has been used. The biogalvanic cell may be the choice for affecting the viability and fertilizing ability of spermatozoa inside the vas lumen[33]. Based on this principle, Misro et al[37] developed non-occlusive male contraceptive devices using different combinations of materials, such as, copper, silver, copper-aluminium, silver-aluminium, silver-graphite and graphite-aluminium. The graphite-aluminium combination was found to be the most effective. This device in rats produced infertility, when the shorting link was closed, leading to current flow. Fertility was restored upon disconnecting the shorting link. The device can be designed in such a way that the closing and opening of the shorting link can be done through the intact scrotal skin by palpation[33]. It is a T shaped device implanted in the vas, made of The device is inert and mechanically sound. The cross-bar of the T is approximately 1. A perforated ball in the T can be rotated by turning the upright arm of T. Alignment of the perforation in the ball with the lumina of the cross bar allows sperm to flow through the device. The device is covered with a fine lattice of gold to allow tissue ingrowth from the de-epithelialized end of vas lumen on to the surface of the device. The method was successful in the human. When the plunger is pushed down, the communication between the tubes is blocked and azoospermia is

obtained. When the plunger is pulled up, spermatozoa will pass through. The device is implanted bilaterally between the cut ends of the vas deferens through a high scrotal incision. Manipulations of the plunger is possible either by palpation on the scrotal skin or through a small scrotal incision. Tantalum clips on the vas deferens of dogs produced azoospermia for a short period but leakage of spermatozoa ensued thereafter[40]. In rabbits azoospermia was reported for a 15 month study period[41]. However, the hope of easy removal of the clips for restoration of fertility was not supported by actual experience. It is a further improvement on the no-scalpel technique and is claimed to be completely non-surgical[42,43]. One major disadvantage, however, with this method is that it is a delicate procedure and requires training and precision. Initially a combination of carbolic and n-butyl alpha cyanoacrylate has been tried in over , men. Studies on pharmacological, toxicological and clinical effects have shown that this compound has no toxic or carcinogenic effects in experimental animals. Ten-year follow up of cases found no long-term complications. The method has cleared WHO toxicological tests[49]. Five per cent sodium morrhuate and potassium permanganate were shown to be ineffective in producing complete sterility while the other agents resulted in complete sterility eight months following a single injection. The lumen of the vas deferens was damaged and replaced by scar tissue and was free of spermatozoa. Dixit et al[53] described that this procedure leads to testicular atrophy and impairment of Leydig cell function. Gallegos et al[54] however, reported that a potent phlogogenic agent, carrageenan, did not produce any effect in the treated animals. The common tissue adhesive, methyl cyanoacrylate has also been shown to produce complete vas occlusion in 60 days in rhesus monkeys[56]. In another approach, a single intravasal administration of 50 L neem oil, injected bilaterally, induced sterility in rats. The histology of the epididymis and vas deferens was normal without any inflammatory reaction or obstruction. No anti-sperm antibodies could be detected in the serum. Unilateral administration of neem oil in the vas resulted in a significant reduction of testicular size and spermatogenic block which only occurred on the side of application. The draining lymph node cells of the treated side showed an enhanced proliferative response to in vitro mutagen challenge. Male fertility regulation by intravasal injection of controlled-releasing gossypol has also been reported[61]. In China before , over 12, men have been using the elastomer. However, as it is a total vas occlusion, the body system is likely to develop anti-sperm antibodies, leading to irreversibility even after plug removal. Such a critical analysis has not been made available[65]. Another shortcoming is that the plug may lead to rupture of the vas[64]. Toxicological uncertainties about the presence of aromatic amines in polyurethane plugs have also been raised, but follow up of acceptors of the method has not so far revealed any justification for this concern[63]. As an alternative, intravasal injection of formed-in-place silicone rubber for vas occlusion has been tried in a small number of human volunteers[66,67]. Azoospermia was obtained after 5 months in 3 men and by 9 months in all men[66]. It is claimed that silicone rubber does not interfere significantly in vas physiology and once the plug is removed, the mucosa cells of the vas will soon regenerate to allow free flow of spermatozoa[24,67]. However, details regarding the reversibility trial of silicone rubber vas occlusion are thus far not available. The main advantage of this method over injectable plugs is its double design. It is composed of two silicone plugs with nylon tails to help anchor the plugs to the vas, thus giving it the potential to be more leak free, i. Double plugs could be more reliable than the single one[20]. The Shug can be inserted into the vas by the no-scalpel method. Full return of fertility after seven months of Shug use has been reported in monkeys[69]. The Shug has several advantages: The preformed plug also avoided the possibility of entry of toxic substances during the hardening processes as in the case of injectable silicone rubber[68]. The efficacy of SMA as an intravas contraceptive has been tested in albino rats[71,72,77] and in rabbits and monkeys[73,74,78,79]. In all subjects, the treatment led to azoospermia and gave pregnancy protection for the one year study period. A non-invasive reversal procedure which involves palpation, percutaneous electrical stimulation, forced vibratory movements in the vas segments and supra-pubic percussion, has also been proposed[90]. References [1] Handelsman DJ. Int J Androl ; 23 suppl 2: Current challenges of andrology. Asian J Androl ; 1: The contribution of asian scientists to global research in andrology. Current status in development of male contraceptives. Current status in fertility regulation:

Constraints in the development of contraceptives for men. Asian J Androl ; 3: Asian J Androl ; 2: Clinical studies using androgens alone for male contraceptive development. Rajalakshmi M, Griffin PD, editors. New Age Int P Ltd; Regulation of male fertility. Martinus Nijhoff ; Knobil E, Neill JD, editors.

Chapter 6 : Bibliomed â€“ 11 - Bibliografia - 1Âª Parte - artigo mÃ©dico de revisÃ£o para pesquisa e consu

In Fertility Regulation Today and Tomorrow (ed E Diczfalusy, M Bygdeman) Serono Symposia Publications, Vol 36, p Raven Press, New York, 19 Rabe T, Kiesel L, Kellermann J, Weidenhammer K, Runnebaum B, Potts GO: Inhibition of human placental progesterone synthesis and aromatase activity by synthetic steroidogenic inhibitors in vitro.

Needs for institutional support in developing countries. Pages in E. Diczfalusy, editor; and A. Some Questions and Answers. Immunologic approaches to fertility regulation. Pages in Stephen L. Corson, editor; , Richard J. Derman, editor; , and Louise B. Little, Brown and Company. New insights on the mode of action of intrauterine contraceptive devices in women. Fertility and Sterility American Fertility Society Ethical considerations of the new reproductive technologies. Restatement of the Law, Second, Torts. American Law Institute Publishers. Anand, Nitya, and V. Role of the pharmaceutical industry of the developing countries in research on fertility regulation. Volume 2, Background Papers. Cases and Materials on Family Law, 2nd ed. Law, Science and Medicine. Law, Science and Medicine: Status of funding and costs of reproductive science research and contraceptive development. Pages in Contraception: Science, Technology, and Application. National Academy of Sciences. Worldwide trends in funding for contraceptive research and evaluation. The next contraceptive revolution. Prospects for improved contraception. Public sector contraceptive development history, problems and prospects for the future. Technology in Society 9: An antiprogestin steroid with contraceptive ability in women. Long-acting injectable Norethistenone contraceptive system: Review of clinical studies. Research Frontiers in Fertility Regulation 3 2: National family planning programs: Pages in S. Behrman, editor; , L. Corsa, editor; , and R. University of Michigan Press. Demographic Requirements of Fertility Control Technology: Food and Drug Administration requirements for toxicity testing of contraceptive products. Acta Endocrinologica 75 Suppl. Black Families in White America. Paper presented at the annual meeting of the Southern Regional Demographic Group. Unmasking the test for design defect: From negligence [to warranty] to strict liability to negligence. Vanderbilt Law Review Black, Henry Campbell Evaluating Unmet Need for Contraception. Staff Working Paper, No. The World Bank, Washington, D. Spermicidal contraceptives and poor reproductive outcomes: The epidemiologic evidence against an association. American Journal of Obstetrics and Gynecology Vaginal spermicides and congenital disorders: Study reassessed, not retracted. Journal of the American Medical Association Research Technology Management 31 4: Highlighting some feminist issues. Successfully meeting regulatory demands to commercialize medical devices. Food, Drug and Cosmetic Law Journal Determinants of Fertility in Developing Countries. Bureau of National Affairs Product Safety and Liability Reporter 15 7 February Pages in T. Is the Asian family planning model suited to Africa? Studies in Family Planning 19 1: The Transdermal Therapeutic System: Sources of the crisis in liability insurance: Yale Journal of Regulation 5: Contraceptive Research and Development Program: Bruce Schearer, and Jean Strand Contraceptives and Drug Regulation: American Bar Association Journal 72 July 1: Termination of early pregnancy by the 3-Hydroxysteroid Dehydrogenase inhibitor Epostane. New England Journal of Medicine Theory, Evidence and Public Policy. Liability Insurance for Contraceptives: Problems in Cost and Availability. The shield intrauterine device. American Journal of Obstetrics and Gynecology 3 February 1: Sri Lanka Contraceptive Survey: Contraceptive futurology or in Contraception 31 1 January: Regulation of Human Fertility. Fertility Regulation Today and Tomorrow. Law, Politics and Birth Control. University of Illinois Press. Research activity on systemic contraceptive drugs by the U. Birth control after A new look at contraceptive testing. The Politics of Contraception: Future methods of fertility regulation in developing countries: How to make the impossible possible by December 31, Searching for ideal contraceptives. Contraception in the year Pages in Pieter A. Pages in Robert Repetto, editor. Development and Testing of Vaginal Contraceptives:

Chapter 7 : Birth control vaccines. | calendrierdelascience.com

Contragestion by antiprogestin RU a novel approach to human fertility control. Fertility Regulation Today and Tomorrow, E. Diczfalusy, M. Bygdeman. Serono Symposia 36, Raven Press, New York ; 55 -

Volume 3 - Danto, Arthur C. Reality of Illusion This list is our complete catalog of items available. In some cases, we have additional copies. To purchase an item, click the item number or enter it on our Search Page. Volume 3 - Banerjea - Coordination Chemistry Milik - Discoveries in the Judaean Desert. Qumran Cave I - Beltrami - Missionari Italiani: Profili di Grandi Apostoli - Plempel - Sterol Biosynthesis Inhibitors: Pharmaceutical and Agrochemical Aspects. Ellis Harwood Series in Biomedicine - Gold - Advances in Physical Organic Chemistry. Volume 15 - Des ouvrages importants dont les auteurs sont nes aux 16e. Taylor - Organic Materials and Fullerenes. Bosman - Display Engineering: Conditioning, Technologies, Applications - Bruce Montgomery - Solenoid magnet design: The magnetic and mechanical aspects of resistive and superconducting systems - Proceedings of a Conference held at Dubrovnik, Yugoslavia, November , Lecture Notes in Mathematics - Materials Performance and Conservation: Published in Commemoration of the Fortieth Anniversay of D. Brugmans - Verzameling Amsterdam. Harold and Jane Hirsh Symposium 1st: Washington - The For-Profit Hospital: Smart - Telling Stories, Secret Lives - Carlos Seco Serrano ed - Andres Muriel: Historia De Carlos IV. Cayetano Alberto De La Barrera - Mattei - Formes Integrables Holomorphes Singulieres. Asterisque, 97 - II, Systems Science ; V. Coffey , David E. Pines , Kevin S. Robert Schrieffer - High Temperature Superconductivity: The Los Alamos Symposium, - Predigten und Ansprachen gehalted in Leipzig bei Ausbruch des Krieges am 2. Eley , Herman Pines - Advances in Catalysis: Volume 33 - Eley, Herman Pines, Paul B. Weisz - Advances in Catalysis, Volume 32 - Weisz - Advances in Catalysis, Volume 31 - Eley, Herman Pines, Werner O. Haag - Advances in Catalysis, Volume 40 - Khanna - Sustainable development: Environmental security, disarmament, and development interface in South Asia - December 3, - June 25, , No. An agricultural and family newspaper. Weisz - Advances in Catalysis, Volume 28 - Diekstra - Suicide Prevention: A Holistic Approach - Dilwyn John - Crinoidea, Discovery reports - Eckmann - Seminaire de Probabilites II: Mars - Octobre Lecture Notes in Mathematics 51 - Dubarle - Optimisme devant ce monde - Aniol - Dendrochronology and Archaeology in Europe. Mitteilungen der Bundesforschungsanstalt fur Forst und Holzwirtschaft Nr. Ano XIII - Parallel Architectures and Languages Europe: Proceedings Lecture Notes in Computer Science - Paroisse et Liturgie, No. Fabian Garcia Nocetti , Peter J. Recuerdo de un Homenaje, Asociacion de la Prensa. Zaragoza, Octubre - G Lindsay - Sea-ice atlas of arctic Canada, - Des Faits, des Reflexions. Rapport presente a une reunion u Volksverein a Olten, le 3 Mai - Redmond - Forum and Column Review. The Journal of the Foreign Affairs Circle. Volume 11 - Tucker - Elementary Electrical Network Theory - Wong - Digital Systems Design - Gayle Nelson - Forest to Farm: Early Days in Otonabee, Ontario - Oesterle - Consultationes de Jure Matrimoniali. Giorgio Castellino - La Sacra Bibia: Libro dei Salmi - Graham Pole - I Refer to India - Curiosita e Documenti di Toponomastica Locale. Volume 1, Desde los Origenes Hasta Volume 2, Pre - Renacimiento y Renacimiento. Volume 3, Renacimiento y Barroco. Three Volumes - H Riddle - Our country for the sake of the world: Barkley - From Bachelor to Betrothed - Elletson - Roosevelt and Wilson: Struble - Xenobiotics and Food-Producing Animals: Roberts - Progress in Pesticide Biochemistry. Volume 2 - J Morgan - Social theory and the family International library of sociology - Proceedings Volume - Haring - Das Ratfel des Krieges: Haussinger - pH Homeostasis: Mechanisms and Control -

Chapter 8 : References - Developing New Contraceptives - NCBI Bookshelf

M Bygdeman. Filter your search Serono Symposia Publications from Raven Press: Fertility Regulation Today and Tomorrow Vol 01 May Hardback. Try AbeBooks.

Valles de Bourges, D. They were compared to a control group of IUD users. Significant findings differed between centres. Further changes were observed during the injection interval, some of which were correlated to changes in serum MPA levels. It is concluded that long-term use of DMPA induces moderate changes in lipid metabolism which are unfavourable in terms of risk for atherosclerosis. This should be borne in mind when weighing the overall risks and benefits of this contraceptive method for a potential user. A review of its safety as a contraceptive, carried out by WHO in l , pointed out that limited data are available on its effect on lipid metabolism, particularly with long-term use. Subsequent studies have given contradictory results, possibly because of the various clinical trial designs, methodologies used and populations studied. Under the same conditions, Amatayakul et al. More recently, Barnes et al. In view of these various findings, this study was undertaken to evaluate the effects of DMPA after several years of use for contraception, in different populations worldwide. They were compared to a control group of healthy women volunteers, in the same age group, who were using a non-hormone releasing IUD or barrier methods for contraception. Other recruitment criteria for these control subjects were that: Women were not included in this study if they had any of the following conditions: Control subjects had two blood samples taken, two weeks apart. Total cholesterol, determined by an enzymatic method 9. HDL-C, using precipitation by addition of phosphotungstate and magnesium ions LDL-C, using precipitation by addition of polyvinyl sulphate Total triglycerides, determined by an enzymatic calorimetric method The cholesterol assays and the triglycerides assay were performed with reagents from Boehringer Mannheim, Federal Republic of Germany. Apofilms and reagents from Sebia, France, were used for the apolipoprotein assays. All the laboratories participated in a lipid standardization programme conducted by the clinical chemistry reference laboratory of Algemeen Ziekenhuis Sint Jan in Brugge, Belgium. After an initial workshop in Brugge, to review the methodology of each assay, several months were spent setting up the assays in each laboratory and instituting internal and external quality control monitoring. The interlaboratory coefficients of variation measured through regular external quality control exercises varied between 2. It should be noted that the samples used for these exercises were lyophilized specimens and that few of them were fully satisfactory for HDL-C and LDL-C assays. The centres noted consistently a much greater reproducibility in their measurements on fresh serum specimens. With internal quality controls, coefficients of variation varied between 0. In addition, serum haemoglobin and fasting glucose were measured on admission in all subjects. Statistical orocedures Either the t-test or analysis of variance was used to determine the significance of differences in individual characteristics on admission between the DMPA users and Contraception controls within each centre, and between the three centres within each group. Comparisons between groups and centres with respect to Serum lipid levels on admission were made by means of analysis of covariance, with number of alcoholic drinks per week, number of cigarettes smoked per day, and Quetelet index as the covariates. Changes in serum MPA and lipid levels in the DMPA users, over the week injection interval, were analyzed by repeated measures analysis of variance. There were significant differences between groups within two of the centres, and between centres within each group Table I. The two groups were similar in age but the DMPA users were heavier and shorter, and thus, had a significantly higher Quetelet index than the controls. Both groups were similar with respect to weight, height, Quetelet index and blood pressure. The DMPA users were approximately 3 years younger than the controls and were almost twice as likely to smoke cigarettes, but these differences were not statistically significant. The DMPA users were significantly older than the controls, by more than 6 years. There were a number of differences between the subjects recruited in the three centres. The DMPA users in Christchurch were also taller and more likely to drink alcohol than those of the other centres. Control subjects in Christchurch were

older than those in Bangkok or Mexico City. After adjusting for alcohol drinking, smoking and Quetelet index, there were some significant differences in serum lipid levels between the study groups in each centre, but these were not consistent between centres Table II. Smoke cigarettes D 0. The differences between the study groups were marked between centres. Control subjects differed in total cholesterol, triglycerides, HDL-C and all three apolipoproteins. In Bangkok and Christchurch, serum MPA levels were significantly higher at 2, 4 and 8 weeks post-injection than pre-injection and they had returned to pre-injection levels by the 13th week. In Mexico City, they rose above the pre-injection level, only at the 2-week follow-up. There was no correlation between these changes and the variations in serum MPA levels measured during the injection interval in these women. The same analysis for the data obtained in Christchurch is shown in Table IVb. In all three centres, the lipid measurements returned to pre-injection levels by the thirteenth week. Although significant findings differ between centres, a pattern of lipid changes can be seen among DMPA users. There were some differences in the characteristics of the women enrolled in the two study groups in each centre. In Bangkok, the DMPA users had a higher Quetelet index than the control subjects, in Mexico they were older by six years on average and in Christchurch they were almost twice as likely to smoke cigarettes. Yet, controlling for these factors, some of the lipid differences noted between the two study groups on admission remained statistically significant and attributable to DMPA use. In further support of an effect of DMPA, is the fact that the differences in lipid profile observed between DMPA-treated women and control subjects on admission are similar in three widely different populations, and that further lipid changes are observed over the DMPA injection interval, some of which are correlated to variations in MPA serum levels. It has now been well demonstrated that LDL-C is a causative agent in the process of atherosclerosis while HDL-C and apolipoprotein AI are recognized as negative, and apolipoprotein B as positive risk indicators for this disorder. However, lipid metabolism is only one of the factors influencing atherosclerosis and previous studies 16,17 comparing the effects of MPA to those of other hormonal contraceptives on lipid metabolism have suggested that MPA Contraception is more beneficial in this respect. Thus, before a woman initiates DMPA use, possible effects on lipid metabolism must be taken into account in weighing the overall balance of risks and benefits of treatment. Her existing underlying risk for atherosclerosis should be assessed from clinical history and her lipid profile obtained in high risk cases. The data presented here further emphasize regional differences that should be noted when comparing results from different centres. This factor complicates interpretation of data but cannot be ignored. Previous studies 18 have consistently shown that, for a same dose of DMPA, Mexican women have lower peak values and a longer half-life than Thai women. The data also show that measurable levels of MPA are found at the time of the next injection, with marked inter- individual variations. This confirms the findings of previous studies 19 that, at a dose of mg, the duration of action of DMPA exceeds three months and there is a build-up of the drug with time. Thus, work should continue to improve the formulation of DMPA in order to bring the dose necessary for effective contraception to the lowest dose possible, and thereby decrease its effect on lipid metabolism. Facts about injectable contraceptives: Memorandum from a WHO meeting. Bull World Health Organization ; A study of glucose tolerance, serum transaminase and lipids in women using depot- medroxyprogesterone acetate and a combination type oral contraceptive. Effects of medroxyprogesterone acetate on serum lipids, protein, glucose tolerance and liver function in Thai women. Alterations in blood lipids and side-effects induced by depo-Provera in Nigerian women. Long-term effects of depo-Provera on carbohydrate and lipid metabolism. Serum high density lipoprotein cholesterol levels in women using a contraceptive injection of depot-medroxyprogesterone acetate. Comparison of lipid and androgen levels after conjugated estrogens or depo-medroxyprogesterone acetate treatment in postmenopausal women. Obstet Gynecol ; Effect of long-term hormonal contraception on plasma lipid. Enzymatic determination of total serum cholesterol. Clin Chem ; Clin Chim Acta ; Bucolo G, David H. Quantitative determination of serum triglycerides. Some considerations of methodology and standardization of apolipoprotein B immunoassays. Evaluation and standardization of apolipoprotein AI immunoassays. Laboratory method manual for the radioimmunoassay of

levonorgestrel, norethisterone and medroxyprogesterone acetate. Lipid metabolism studies in oophorectomized women. Effects of three different progestogens. Acta Obstet Gynecol Scand Suppl ; Different effects of two progestins on plasma high density lipoprotein HDL2 and post-heparin plasma hepatic lipase activity. Dicfalusy E and Bygdeman M, eds. Fertility Regulation today and tomorrow. Raven Press, Serono Symposia Long-term effects of depot-medroxyprogesterone acetate on lipoprotein metabolism.

Chapter 9 : Fertility regulation today and tomorrow (Book,) [calendrierdelascience.com]

(1st ed.)E Diczfalusy, M Bygdeman (Eds.), Fertility Regulation Today and Tomorrow, 36, Serono Symposia Publications: Raven Press (), pp. 8. Sheng-cai Zhao Research on reversible blocking of the spermatic duct using injected MPU.

Some metabolic and hormonal changes in women using long acting injectable contraceptives. Alexandria Journal of Pharmaceutical Sciences 3 1: Determinants of acceptance of injectable contraception in Bangladesh. The effects of Depo-Provera on carbohydrate, lipids and vitamin metabolism. Journal of Steroid Biochemistry 11 1B: Effects of medroxyprogesterona, acetate on serum lipids, protein, glucose tolerance and liver function in Thai women. A study of the mechanism of weight gain in medroxyprogesterone acetate users. Counseling about side effects improves contraceptive continuation Network 12 2: Beagle carcinogenicity studies no, longer required for Progestogens. Acceptability of injectable contraception in the Philippines. An overview of the FPNP injectable programme. Recent advances in contraceptive technology: Proceedings of the seminar held Oct. Monthly injectable contraceptives and breast cancer. Injectable Contraceptives, [Video] Washington, D. Ellis, Ellis Pharmaceutical Consulting, May 31, Risk of human immunodeficiency virus and Hepatitis-B vim transmission through unsafe injections: A new class of potent progestins. Journal of the American Chemical Society 80 pt. Analyse, situationnelle du programme da planification familiale au Burkina Faso. Department of Health, Feb. Studies in Family Planning 9 Return of fertility following discontinuation of an injectable contraceptive-Norethisterone oenanthate NET EN mg dose. Bangladesh Demographic and Health Survey A study of women who conceived after discontinuation of Depo Provera. Review of ovulation return upon discotinuation of once-a-month injectable contraceptives. A comparative study on the return to ovulation following chronic use of once-a-month injectable contraceptives. Determinants of menstrual bleeding patterns among women using natural and hormonal methods of contraception: The influence of individual characteristics. The analysis of menstrual bleeding patterns: The analysis of vaginal bleeding patterns induced by fertility regulating methods. The association between vaginal bleeding patterns and reasons for discontinuation of contraceptive use. Depo medroxyprogesterone acetate Depo Provera for contraception. Benson and Pernolls handbook of obstetrics and gynecology. New York, McGraw-Hill, Improving contraceptive supply management. Family Planning manager 1 4: Depot medroxyprogesterone acetate Depo-Provera as a contraceptive preparation. South African medical journal 45 Oral contraception and congenital malformations in offspring A review and meta-analysis of the prospective studies. Acceptability of Depo-Provera as a reliable contraceptive method. Amsterdam, Excerpta Medica Foundation, Contraceptive use and breast- Feeding duration in rural Bangladesh. European Journal of Clinical Nutrition 45 7: Anaphylactoid shock with medroxyprogesterone acetate: Short term increase in risk of breast cancer after full term pregnancy. British Medical Journal What does the Matlab fertility experience really show? National Centre for Epidemiology and Population Health, Alterations in blood sugar, protein, and lipid levels in Indian women by norethisterone enanthate. International Journal of Fertility 32 3: Proceedings of the symposium Progesterone, progestins, and fetal development. Fertility and Sterility 30 1: New regimen of injectable contraceptives. Journal of the Medical Association of Thailand 70 4: Concentration of fat, protein, lactose and energy in milk of mothers using hormonal contraceptives. Annals of Tropical Paediatrics 12 2: Manila Bulletin, May 1, A prospective study of adolescents who choose among levonorgestrel implant Norplant , medroxyprogesterone acetate Depo-Provera , or the combined oral contraceptive pill as contraception. Fertility regulation today and tomorrow, New York, Raven, Serono Symposia Publications Vol. Bone density in women receiving depot medroxytrogesterone acetate for contraception. A changing pattern in the association of oral contraceptives and the different groups of congenital limb deficiencies. WHO [injectable research] Personal communication, Mar. Some effects of depo-medroxyprogesterone acetate DMPA: Observations in the nursing infant and in the long-term user. International Journal of Gynaecology and Obstetrics 20 1: Vaginal bleeding patterns of women using different contraceptive methods implants, injectables, IUDs, ml

pills An Indian experience. Geburtshille und Frauenheilkunde 17 Medroxyprogesteronee acetate and homozygous sickle-cell disease. Quality of care in family planning in Latin America. Advances in Contraception 9 2: Diseases of the breast. Depo-provera medroxyprogesterone acetate for contraception: A current perspective of scientific, clinical and social issues. Proceedings of an international symposium held on Nov. Oxford, England, Oxford Clinical Communications, A partnership for urban health and family planning in Bangladesh. An asessment of programme needs in zone 3 of Dhaka City. Ministry of Health and Family Welfare. Long-term use of depot medroxy progesterone acetate as a contraceptive. Acta Obstetricia et Gynecologica Scandinavia Egypt Demographic and Health Survey A prospective, one-year study on the effects of two long acting injectable contraceptives depot-medroxyprogesterone acetate and norethisterone oenanthate on serum and lipoprotein lipids. Hormone and Metabolic Research 24 2: Effect of long-acting progestagen-only injectable contraceptives on carbohydrate metabolism and its hormonal profile. Effect of depo-medroxyprogesterone acetate on coagulation factors and serum lipids in Egyptian women. Alterations in blood lipids and side effects induced by Depo-Provera in Nigerian women. The effects of depo-provera on serum protein levels in Nigerian women. Journal of Steroid Biochemistry 20 2: Experience with the use of depo-medroxyprogesterone acetate in a Nigerian population. African journal of medicine and Medical Sciences 17 4: Contraceptive Technology Update Series Pesquisa sobre sade familiar no Nordeste Brasil Injectables use increasing rapidly. Factors affecting the duration of action at the injectable contraceptive norethisterone enanthate. Contraceptive Delivery Systems 2 3: A preliminary pharmacological trial of the monthy injectable contraceptive Cycloprovera. Return of ovulation and fertility in women using noreshisterone oenanthate.