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A REVIEW OF NATURAL STEROIDS AND THEIR APPLICATIONS

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ABSTRACT

Natural steroids, the simple mention of the word brings up topics like cheating, unfair advantages. The first misconception is that all steroids are used for muscle building. This is not at all the case, steroids are natural substances with many different effects in the human body, which begin over several days, as even birth control pills are a form of steroids. "Natural Steroids", are the organic compounds which are not chemically altered, that mimics hormones, and obviously the hormone it mimics is testosterone. Natural Steroids are involved in a wide range of physiologic processes, including stress response, immune response, carbohydrate metabolism, protein catabolism, blood electrolyte levels, and in the regulation of inflammation, and behavior. The uses are far outreach simply bulking up on muscle. Natural steroids can be used to increase certain enzymes a person's body may have trouble creating naturally, such as testosterone, which is vital in the development in growing men.

INTRODUCTION: Steroids naturally occur in the human body; natural steroids are produced in the body by in-which they use protein in order to build muscle tissue. Although the process is far more in-depth than that, in general terms this is what occurs.

Steroids constitute an important class of hormones. Hormones are chemical compounds that are produced by specialized cells in the body and are released into the circulatory system. When these compounds reach their target cells, they interact with hormone receptor proteins and elicit specific physiological responses. In the case of steroid hormones, the physiological response is achieved by regulating the expression of specific genes [1].

The natural steroids are commonly used in medicine because they allow physicians to elicit the specific responses from tissues.

One steroid commonly used is cortisol, a natural steroid hormone produced by the adrenal gland in response to stress. This hormone brings about an increase in blood pressure and blood sugar levels and also prevents inflammation in target tissues. The anti-inflammatory properties of cortisol make it particularly useful medicinally. Cortisol is used in ointments to treat skin ailments and in inhalers to treat asthmatic attacks. It is also used in injections to control swelling resulting from injuries and to reduce the inflammation associated with arthritis.

Other commonly used steroid hormones include progesterone (a progestin steroid) and estradiol (an estrogen steroid). Progesterone controls events during pregnancy, and estradiol regulates female characteristics. Both of these steroid hormones are components of birth control pills and function by preventing ovulation.

Anabolic steroids are refer to hormones. Several hormones in this family are naturally produced by the body in order to maintain male characteristics and to promote muscle and bone growth. These steroids are mainly used in medicine to fight the effects of chronic wasting disease and the late stages of AIDS as well as to treat osteoporosis.

Anabolic steroids are either taken orally or by injection that influence the body's hormonal system to produce extra testosterone. The goal of taking anabolic steroids is to increase muscle mass. Anabolic refers to this muscle-building capability. Anabolic steroids should not be confused with corticosteroids, which are used routinely as anti-inflammatory medications to help treat illnesses in which inflammation is part of the disease process [1].

Classification of Steroids: Some of the common categories of steroids:

- Animal
  - Insect
    - Ecdysteroids such as ecdysterone
  - Vertebrate
    - Steroid hormones
    - Sex steroids are a subset of sex hormones that produce sex differences or support reproduction. They include androgens, estrogens, and progestagens.
    - Corticosteroids include glucocorticoids and mineralocorticoids. Glucocorticoids regulate many aspects of metabolism and immune function, whereas mineralo-corticoids help maintain blood volume and control renal excretion of electrolytes. Most medical 'steroid' drugs are corticosteroids.
    - Anabolic steroids are a class of steroids that interact with androgen receptors to increase muscle and bone synthesis. There are natural and synthetic anabolic steroids. In popular language, the word "steroids" usually refers to anabolic steroids.
    - Cholesterol, which modulates the fluidity of cell membranes and is the principal constituent of the plaques implicated in atherosclerosis.
- Plant
  - Phytosterols

Examples of phytosterols are, Beta-Sitosterol, Stigmasterol

  - Brassinosteroids

Examples of Brassinosteroids are Campesterol

- Fungus
  - Ergosterols

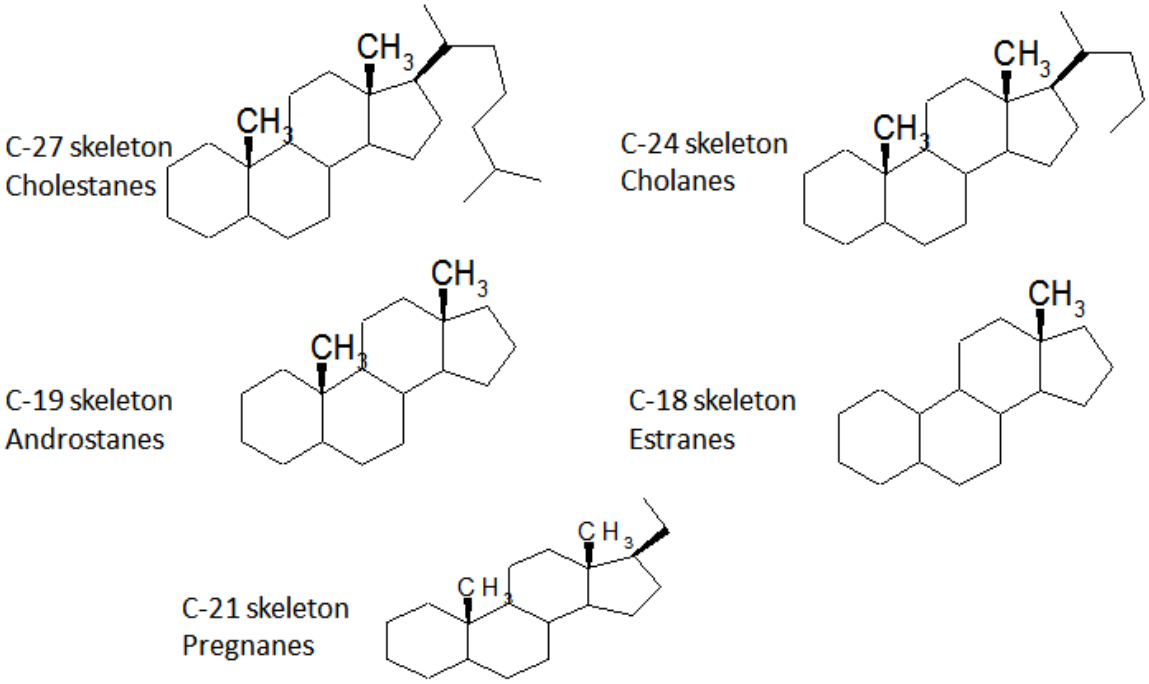
Examples of Yeast

Structural: It is also possible to classify steroids based upon their chemical composition. One example of how MeSH performs this classification is available at the Wikipedia MeSH catalog. Examples from this classification include:

Class	Examples	Number of Carbon Atoms
Cholestanes	Cholesterol	27
Cholanes	Cholic Acid	24
Pregnanes	Progesterone	21
Androstanes	Testosterone	19
Estranes	Estradiol	18

Gonane (or steroid nucleus) is the parent (17-carbon tetracyclic) hydrocarbon molecule without any alkyl sidechains [2].

Number of Nuclear positions and Steroid classification:



1. **Steroids as Anticancer Agents:** Corticosteroids are commonly used in the treatment of patients with advanced cancer. However, much of this use stems from the experience of practitioners rather than from data collected in controlled clinical trials. Although little is known about the actual mechanisms by which corticosteroids exert their effects in patients, a substantial amount of evidence supports their monitored use in specific situations. This article will review the available evidence on the use of corticosteroids in advanced cancer, including treatment of refractory malignancies, use as premedication with chemotherapy, and symptom palliation [3].

Background Information: The most commonly used corticosteroids in the United States include prednisone, prednisolone, methlyprednisolone, dexamethasone, and hydrocortisone, all of which were approved by the Food and Drug Administration in the 1950s. There does not appear to be evidence to support the use of one corticosteroid over another in any given situation, although physicians have their preferences. Corticosteroids exhibit varying glucocorticoid and mineralocorticoid effects. More potent glucocorticoid effects are desirable in inflammatory states, whereas mineralocorticoid effects are needed to treat adrenal insufficiency. Corticosteroids inhibit inflammatory and immune responses, most likely through alteration of cellular transcription and protein synthesis as well as through effects on lipocortins, which inhibit the release of arachidonic acid. The use of corticosteroids in advanced cancer revolves around their glucocorticoid effects, combined with an avoidance of the salt-retaining properties that characterize mineralo-corticoids. That said, it is important to remember that patients previously treated with corticosteroids may have some degree of adrenal suppression and, therefore, may require supplemental corticosteroid therapy during stressful situations. In this setting, mineralocorticoid properties are desired.

Effects of Long-Term use: Chronic use of corticosteroids causes adrenal suppression and may blunt or prevent normal adrenal response to physiologic stress. To avoid this effect, many cancer patients may receive intermittent doses of steroids as antiemetic to prevent hypersensitivity reactions, or as adjuvants for pain control. Spiegel and colleagues performed Adreno Cortico Tropic Hormone (ACTH) - stimulation tests in 14 patients receiving high-dose prednisone for emesis prophylaxis prior to chemotherapy. Adrenal function was suppressed in 13 patients at 24 hours and remained suppressed in 5 patients for more than 1 week. Investigators at the University of Rochester performed ACTH-stimulation tests in nine women with ovarian cancer before and during chemotherapy in which dexamethasone pre-

medication was used. They noted effects on the hypothalamic-pituitary axis for up to 8 days, but reported no long-term suppression. It is probably not necessary to taper steroids when they are administered in brief, intermittent doses, but adrenal suppression should be considered when patients who have received such treatment present with hypotension and severe illness. The use of replacement-dose steroids in patients with cancer who are undergoing surgery was recently reviewed by Lefor.

The risks associated with corticosteroid use in patients with advanced cancer have been reviewed extensively. Acute side effects include dyspepsia, peptic ulcer disease, insomnia, oral and vaginal candidiasis, anxiety, and glucose intolerance. Side effects from chronic use include development of a cushingoid appearance, weight gain, edema, cataracts, osteoporosis, proximal myopathy, thinning of the skin, infection, and impaired wound healing. Corticosteroids can also lead to neuropsychiatric changes including depression, agitation, and delirium. It is important, therefore, to carefully weigh the potential benefits of corticosteroid therapy against potential side effects, and to closely monitor the efficacy of therapy. If no improvement is noted, treatment should be adjusted or discontinued [4].

2. **Corticosteroids as Anticancer Agents:** Corticosteroids have been used as anticancer agents since the 1940s, with activity reported in a wide variety of solid tumors, including breast and prostate cancer, and the lymphoid hematologic malignancies. They are commonly found in regimens for acute lymphocytic leukemia, Hodgkin's and non-Hodgkin's lymphoma, myeloma, and chronic lymphocytic leukemia. This section will focus on the use of corticosteroids as palliative anticancer treatment once chemotherapeutic options have been exhausted or abandoned.

Multiple Myeloma: Several studies have been reported suggesting a benefit with the use of corticosteroids in refractory multiple myeloma. Alexanian reported the use of pulse prednisone therapy in patients with myeloma refractory to melphalan. Prednisone was administered at 60 mg/m^2/d for 5 of 8 days, for three pulses followed by a 3-week rest, with the cycle repeated. The investigators noted a greater than 50% reduction in tumor mass in 5 of 16 patients, and found that responding patients benefited clinically with less pain, improved performance status, and increased hemoglobin. Norfolk and Child performed a similar study in 17 patients with relapsed or refractory disease. Patients in this study received prednisolone, 60 mg/m^2/d for 5 days, followed by a 9-day rest. Fourteen patients completed six cycles of treatment, and 10 had more than a 25% reduction in serum paraprotein or a 50% reduction in urinary light-chain excretion. An overall improvement in quality of life was also noted. Notably, two of the nonresponders demonstrated an improvement in performance status. Median survival for the group was more than 19 months.

In 1991, the Eastern Cooperative Oncology Group reported a pilot study of high-dose, pulsed dexamethasone in patients with relapsed or refractory disease. Patients received dexamethasone, 40 mg/d, 4 days a week for 8 weeks. Of 32 patients enrolled, 13 (40%) achieved objective responses and 28.5% showed improvement in pain or performance status. The study also reported significant toxicity, with 19 patients experiencing side effects assessed as at least grade 2. Median survival was 19 weeks, and the authors suggested that less frequent administration at longer intervals should be considered. Alexanian also reported on the use of intermittent, high-dose dexamethasone, noting a 27% response rate in patients who did not respond to their prior treatment.

The Southwest Oncology Group reported a trial of alternate-day administration of corticosteroids (oral prednisone, 100 mg every other day for 2 weeks, then 50 mg every other day for 10 weeks) in 121 patients with relapsed or refractory myeloma. They measured glucocorticoid receptors from patient samples and found an improved response, but no change in overall survival among patients with a moderate number of receptors, compared with patients with a low number of receptors. They reported a 10% partial response rate (defined as a 50% to 75% decrease in M-protein), although 81 patients maintained stable disease while enrolled in the study.

Prednisone, as used in this study, was well tolerated and appeared to be associated with response and median survival rates (12 months) similar to those reported with other drug schedules used in myeloma.

Non-Hodgkin's Lymphoma: In 1996, Newcom reported on the outcome of two patients with refractory, poorly differentiated lymphocytic lymphoma who had been treated with continuous corticosteroids (prednisone, 60 to 100 mg/d). Both patients improved within 3 weeks of the initiation of single-agent prednisone, and both reportedly experienced regression of nodes and organomegaly as well as an improvement in function. However, the patients died 14 and 15 months after initiation of therapy with prednisone.

Breast Cancer: Steroids have been used in the primary treatment of breast cancer in elderly women after failure of front-line hormonal therapy. Minton followed 91 women aged 65 years and older in whom disease progressed following initial hormonal therapy with estrogens, tamoxifen, or androgens. A treatment-free period of 1 month was recommended to control for a withdrawal response. The majority of patients received prednisolone, 15 mg daily, and 10 patients received hydrocortisone acetate, 75 mg daily. Objective responses were noted in 13 patients (14%). Another 19 (21%) achieved stable disease for at least 6 months. There was no correlation with any prior response to endocrine therapy, and toxicity was felt to be acceptable. Unfortunately, the authors did not report a clinical benefit as subjectively reported by the patients.

Mercer and colleagues reported a prospective randomized trial of aminoglutethimide (Cytadren, 125 mg twice daily) vs hydrocortisone (20 mg twice daily) in advanced breast cancer. All patients were postmenopausal and had experienced disease progression on tamoxifen. Of 61 patients entered into the trial, 56 were included in the analysis. Three patients who received aminoglutethimide achieved a partial response (11%), while one partial and five complete responses (21%) were reported in the hydrocortisone group. Although this difference was not statistically significant, it does serve as evidence that corticosteroids have activity in breast cancer. The authors did not report on clinical benefit.

Prostate Cancer: Hormone therapy is well established in the treatment of prostate cancer. However, progressive disease after failure of hormone therapy is a difficult problem for patients in this setting. Tannock and colleagues from the Princess Margaret Hospital in Toronto have reported their experience with prednisone in the treatment of hormone-refractory disease. In an informative study, these investigators prospectively treated 37 men with symptomatic bone metastases with 7.5 to 10 mg of prednisone daily. Pain scores were assessed by three different measures at monthly intervals.

An improvement in all three pain scales without an increase in opiate dosages was reported for a minimum of 1 month in 14 (38%) patients. Responses did not correlate with alkaline or acid phosphatase measures, but did appear to correlate with suppression of adrenal androgens. Although the median duration of response was only slightly more than 4 months, the investigators concluded that there was improvement in quality of life with little toxicity or expense. These investigators have now reported on the superiority of the combination of mitoxantrone and prednisone as palliation for a similar group of patients; however, this therapy was not associated with a survival advantage. Some patients will opt not to receive chemotherapy, although corticosteroids alone may be beneficial.

Sartor and colleagues assessed the effects of prednisone, 10 mg twice daily, on Prostate-Specific Antigen (PSA) in 29 men with progressive, hormone-refractory prostate cancer. Twenty-six of the patients were symptomatic. PSA levels declined by at least 25% in 14 (48%) of the patients, and 23 of 26 reported an improvement in appetite, weight gain, or pain control. The median progression-free survival was 2 months; however, median overall survival was 12.8 months after initiation of therapy with prednisone. The duration of symptom control and any correlation with PSA measurements were not reported, but would be of interest as patients lived an average of 10 months beyond the development of progressive disease [5].

3. **Steroids in Birth Control Pills:** The combined oral contraceptive pill (COCP), often referred to as the birth-control pill or colloquially as "the Pill", is a birth control method that includes a combination of an estrogen (oestrogen) and a progestin

(progestogen). When taken by mouth every day, these pills inhibit female fertility. They were first approved for contraceptive use in the United States in 1960, and are a very popular form of birth control. They are currently used by more than 100 million women worldwide and by almost 12 million women in the United States. Usage varies widely by country, age, education, and marital status: one third of women aged 16–49 in the United Kingdom currently use either the combined pill or a progestogen-only "minipill", compared to only 1% of women in Japan.

Medical Use: Combined oral contraceptive pills should be taken at the same time each day. If one or more tablets are forgotten for more than 12 hours, contraceptive protection will be reduced. Most brands of combined pills are packaged in one of two different packet sizes, with days marked off for a 28 day cycle. For the 21-pill packet, a pill is consumed daily for three weeks, followed by a week of no pills. For the 28-pill packet, 21 pills are taken, followed by week of placebo or sugar pills. A woman on the pill will have a withdrawal bleed sometime during the placebo week, and is still protected from pregnancy during this week. There are also two newer combination birth control pills (Yaz 28 and Loestrin 24 Fe) that have 24 days of active hormone pills, followed by 4 days of placebo.

Placebo Pills: The placebo pills allow the user to take a pill every day; remaining in the daily habit even during the week without hormones. Placebo pills may contain an iron supplement, as iron requirements increase during menstruation. Failure to take pills during the placebo week does not impact the effectiveness of the pill, provided that daily ingestion of active pills is resumed at the end of the week. The withdrawal bleeding that occurs during the break from active pills was thought to be comforting, as a physical confirmation of not being pregnant. The 28-day pill package also simulates the average menstrual cycle, though the hormonal events during a pill cycle are significantly different from those of a normal ovulatory menstrual cycle. The withdrawal bleeding is also predictable; as a woman goes longer periods of time taking only active pills, unexpected breakthrough bleeding becomes a more common side effect.

Less Frequent Placebos: If the pill formulation is monophasic, it is possible to skip withdrawal bleeding and still remain protected against conception by skipping the placebo pills and starting directly with the next packet. Attempting this with bi- or tri-phasic pill formulations carries an increased risk of breakthrough bleeding and may be undesirable. It will not, however, increase the risk of getting pregnant.

Starting in 2003, women have also been able to use a three-month version of the Pill. Similar to the effect of using a constant-dosage formulation and skipping the placebo weeks for three months, Seasonale gives the benefit of less frequent periods, at the potential drawback of breakthrough bleeding. Seasonique is another version in which the placebo week every three months is replaced with a week of low-dose estrogen. A version of the combined pill has also been packaged to completely eliminate placebo pills and withdrawal bleeds. Marketed as Anya or Lybrel, studies have shown that after seven months, 71% of users no longer had any breakthrough bleeding, the most common side effect of going longer periods of time without breaks from active pills.

Effectiveness: The effectiveness of COCPs, as of most forms of contraception, can be assessed in two ways. Perfect use or method effectiveness rates only include people who take the pills consistently and correctly. Actual use, or typical use effectiveness rates are of all COCP users, including those who take the pills incorrectly, inconsistently, or both. Rates are generally presented for the first year of use. Most commonly the Pearl Index is used to calculate effectiveness rates, but some studies use decrement tables. The typical use pregnancy rate among COCP users varies depending on the population being studied, ranging from 2-8% per year. The perfect use pregnancy rate of COCPs is 0.3% per year.

Several factors account for typical use effectiveness being lower than perfect use effectiveness:

- Mistakes on the part of those providing instructions on how to use the method
- Mistakes on the part of the user
- Conscious user non-compliance with instructions.

For instance, someone using oral forms of hormonal birth control might be given incorrect information by a health care provider as to the frequency of intake, or by mistake not take the pill one day, or simply not go to the pharmacy on time to renew the prescription.

COCPs provide effective contraception from the very first pill if started within five days of the beginning of the menstrual cycle (within five days of the first day of menstruation). If started at any other time in the menstrual cycle, COCPs provide effective contraception only after 7 consecutive days use of active pills, so a backup method of contraception must be used until active pills have been taken for 7 consecutive days. COCPs should be taken at approximately the same time every day.

Contraceptive efficacy may be impaired by:

1) Missing more than one active pill in a packet,

2) Delay in starting the next packet of active pills (i.e., extending the pill-free, inactive or placebo pill period beyond 7 days),

3) Intestinal malabsorption of active pills due to vomiting or diarrhea,

4) Drug interactions with active pills that decrease contraceptive estrogen or progestogen levels.

Drug Interactions: Some drugs reduce the effect of the Pill and can cause breakthrough bleeding, or increased chance of pregnancy. These include drugs such as rifampicin, barbiturates, phenytoin and carbamazepine. In addition cautions are given about broad spectrum antibiotics, such as ampicillin and doxycycline, which may cause problems "by impairing the bacterial flora responsible for recycling ethinylestradiol from the large bowel". The traditional medicinal herb St John's Wort has also been implicated due to its upregulation of the P450 system in the liver.

Mechanism of Action: Combined oral contraceptive pills were developed to prevent ovulation by suppressing the release of gonadotropins. Combined hormonal contraceptives, including COCPs, inhibit follicular development and prevent ovulation as their primary mechanism of action.

Progestogen negative feedback decreases the pulse frequency of gonadotropin-releasing hormone (GnRH) release by the hypothalamus, which decreases the release of follicle-stimulating hormone(FSH) and greatly decreases the release of Luteinizing Hormone (LH) by the anterior pituitary. Decreased levels of FSH inhibit follicular development, preventing an increase in estradiol levels.

Progestogen negative feedback and the lack of estrogen positive feedback on LH release prevent amid-cycle LH surge. Inhibition of follicular development and the absence of a LH surge prevent ovulation.

Estrogen was originally included in oral contraceptives for better cycle control (to stabilize the endometrium and thereby reduce the incidence of breakthrough bleeding), but was also found to inhibit follicular development and help prevent ovulation. Estrogen negative feedback on the anterior pituitary greatly decreases the release of FSH, which inhibits follicular development and helps prevent ovulation.

A secondary mechanism of action of all progestogen-containing contraceptives is inhibition of sperm penetration through the cervix into the upper genital tract (uterus and fallopian tubes) by decreasing the amount of and increasing the viscosity of the cervical mucus.

Other possible secondary mechanisms may exist. For instance, the brochure for Bayer's YAZ mentions changes in the endometrial effects that reduce the likelihood of implantation of an embryo in the uterus. Such a secondary mechanism would occur if breakthrough ovulation were to occur and result in a post-fertilization effect.

One example isendometrial effects that prevent implantation of an embryo in the uterus. A scientific analysis of the available studies on this issue concluded "that good evidence exists to support the hypothesis that the effectiveness of oral contraceptives depends to some degree on postfertilization effects. However, there are insufficient data to quantitate the relative contribution of postfertilization effects. Some physicians and patients consider such a mechanism to be abortifacient.

Other scientists point out that the possibility of fertilization during COCP use is very small. From this, they conclude that endometrial changes are unlikely to play an important role, if any, in the observed effectiveness of COCPs. Subsequently, the frequency of such postfertilization mechanisms is a controversial topic and currently unresolved.

Formulations: Oral contraceptives come in a variety of formulations. The main division is between combined oral contraceptive pills, containing both estrogen and progestins and progestin only pills. Combined oral contraceptive pills also come in varying types, including varying doses of estrogen, and whether the dose of estrogen or progestin changes from 1 week to the next.

Non-contraceptive uses: The hormones in "the Pill" can also be used to treat other medical conditions, such as polycystic ovary syndrome (PCOS), endometriosis, adenomyosis, menstruation-related anemia and painful menstruation (dysmenorrhea). In addition, oral contraceptives are often prescribed as medication for mild or moderate acne. The pill can also induce menstruation on a regular schedule for women bothered by irregular menstrual cycles or disorders where there is dysfunctional uterine bleeding. In addition, the Pill provides some protection against breast growth that is not cancer, ectopic pregnancy, vaginal dryness and menopause-related painful intercourse.[6]

4. **Steroids as Anti-Inflammatory Agents:** Early in this century it was discovered that corticosteroid hormones, if purified and taken in large amounts as a medicine, have powerful anti-inflammatory effects. Ever since this discovery, corticosteroids have been used to treat a great variety of diseases where inflammation (not infection and not cancer) is the major problem, from arthritis to psoriasis to asthma. To treat the inflammation of asthma within the bronchial tubes, steroids can be taken in tablet or liquid form or by inhalation. Occasionally, steroids are given by injection or in hospitalized persons directly into the veins (intravenous infusion). Taken as tablets, liquid, injection, or intravenous infusion, the steroid medication travels in the blood and is carried throughout the body, including to the bronchial tubes.

   Used in this way, steroids have their most powerful effects, both for the good (relieving asthmatic symptoms) and for the bad (undesirable side effects). On the other hand, modern steroid medications inhaled on the bronchial tubes from pressurized canisters act directly on these tubes; almost no medication is carried into the bloodstream. Although not as powerful in their immediate effects, steroids by inhalation are better suited for long-term use in the treatment of inflamed bronchial tubes because they are free of major undesirable side effects.

Examples of steroids in tablet form are prednisone (Brand name: Deltasone) and prednisolone (Brand-name: Medrol). Examples of steroids by inhalation are triamcinolone (Brand-name: Azmacort); beclo-methasone (Brand-names: Vanceril, Qvar, and Beclovent); flunisolide (Brand-names: Aerobid® and Aerobid-M); fluticasone (Brand-name: Flovent); and budesonide (Brand name Pulmicort).

A Short Course of Steroids: Steroids taken in tablet or liquid form ("oral steroids") are usually prescribed for asthma that has become difficult to control by any other means; they are the most effective treatment available for a severe "attack" of asthma. Most often, they are prescribed for a short period of time: a short course may be as brief as 3-4 days or as long as 2-3 weeks. They are stopped when the asthma has gotten better and other treatments suffice to keep it under control. Longer periods of treatment and continuous treatment with oral steroids are generally avoided except for the most difficult-to-control asthma because of the undesirable side effects that often develop with prolonged oral steroid treatment.

Variable Doses and Schedules: The dose of oral steroids will vary with the severity of the asthma and an individual's sensitivity to the medication. As a rough guide, we consider less than 20 milligrams (abbreviated "mg") of prednisone a low dose, 20 to 30 mg a moderate dose, and 40 to 60 mg a high dose of oral steroids. When rapid relief from an asthma attack is needed, a high dose will often be recommended initially, followed by a gradual reduction in dose on successive days until the oral steroids are stopped: a "steroid taper."

However, when a short course of oral steroids is used, it is not always necessary to taper the dose; a high dose can be safely stopped abruptly (for instance, 40 mg of prednisone taken each day for 3 days, then stopped). There is no single schedule of oral steroid dosing that is right for all asthma attacks in all patients.

Effects of a Short Steroid Course: The beneficial effects of oral steroids are usually evident within several hours. Breathing becomes easier and wheezing, cough, mucus production, and chest tightness all gradually lessen. Other allergic diseases, such eczema and nasal congestion and drip, are also likely to be helped by the anti-inflammatory action of the oral steroids. Many people also find that oral steroids, independent of their effect on breathing, give a powerful boost of energy for a short while.

Steroids, anti-inflammatory drugs such as prednisone, can be used for asthma as well as other lung diseases. Prednisone and other steroids (inhaled, oral, or by injection) help calm airway inflammation in asthma. If you've ever had a serious asthma attack, you may have had high doses of steroids in the hospital administered intravenously.

Prednisone is an oral steroid medication. If you have serious worsening of asthma symptoms (an asthma attack), your doctor may prescribe a brief course of oral steroids such as prednisone. Oral steroids may also be prescribed when your asthma symptoms worsen but you do not require hospitalization [7].

Oral prednisone is a systemic steroid. That means that after taking prednisone by mouth (orally), it goes directly into the bloodstream, unlike inhaled steroids (anti-inflammatory asthma inhalers) that go straight to the lungs. Prednisone and other systemic steroids may be used to treat asthma attacks and help people gain better asthma control. Steroids are used with other asthma medications to either control sudden and severe asthma attacks or to treat long-term, hard-to-control asthma.

Sometimes systemic steroids like prednisone are taken in high doses for a few days. This is called a steroid burst. They may also be given in a low dose daily or every other day for long-term asthma control. While a two-week course or "short burst" of oral steroids like prednisone is relatively safe, it's important to avoid steroids on a long-term basis as there are potential serious side effects. Taking supplemental calcium may help to prevent osteoporosis or thinning of the bones, which is one of the side effects of long-term steroid use.

If you need steroids frequently for "rescue" therapy, this can suggest poor control of airway inflammation or continued exposure to some unsuspected allergen. In this case, talk to your health care provider about inhaled anti-inflammatory medications.

Anti-inflammatory asthma inhalers are the first line of treatment for asthma and may play a role in other lung diseases. In fact, recent studies support the use of anti-inflammatory asthma inhalers early in the course of disease. After introduction of inhaled steroids, the need for oral steroids such as prednisone may decrease.

Unlike the serious side effects of oral steroids, the most common side effects of anti-inflammatory asthma inhalers are hoarseness and thrush, especially in elderly adults. As with all asthma inhalers, you should rinse the mouth carefully after using your inhaler. Gargle with water after inhalation to help reduce the risk of oral thrush [8].

Steroids to Treat Arthritis: Steroids often are injected directly into joints to treat conditions such as rheumatoid arthritis, gout, or other inflammatory diseases. They also can be injected into an inflamed bursa or around tendons near most joints in the body. Some people report relief from osteoarthritis when steroids are injected directly into swollen or painful joints. Steroid injections into a specific area are generally well tolerated and are less likely than other forms of steroid drugs to produce serious side effects.

Also, the injections may help avoid the need for oral steroids or increased doses of oral steroids, which could have greater side effects. Steroid injections can be added to a treatment program that may already include anti-inflammatory pain medications (NSAIDs), physical therapy, occupational therapy, or supportive devices such as canes and braces. Whether one or more of these treatment methods are used depends on the nature of the problem.

For example, in an otherwise healthy person, tendinitis may be adequately treated with only a steroid injection into the inflamed area. However, in a person with rheumatoid arthritis, injections are generally a small part of a multifaceted treatment approach.[9]

Steroids should not be injected when there is infection in the area to be targeted or even elsewhere in the body because they could inhibit the natural infection-fighting immune response. Also, if a joint is already severely destroyed, injections are not likely to provide any benefit.

If someone has a potential bleeding problem or is taking anticoagulants often referred to as blood thinners, steroid injections may cause bleeding at the site. For these people, injections are given with caution.

Frequent steroid injections, more often than every three or four months, are not recommended because of an increased risk of weakening tissues in the treated area. Steroid injections are one of the most effective ways to decrease pain and improve function, yet they generally do not cure the illness.

In rare instances, the following side effects might occur:

- Infection
- Allergic reactions
- Bleeding into the joint
- Rupture of a tendon
- Skin discoloration
- Weakening of bone, ligaments, and tendons (from frequent, repeated injections into the same area)

Not everyone will develop side effects and side effects vary from person to person. If steroid injections are infrequent (less than every three to four months), it is possible that none of the listed side effects will occur. If steroid use is brief (from a few days to a few weeks), it is possible that none of the listed side effects will occur. The side effects listed generally do not occur when occasional steroid injections are given for arthritis, tendinitis, or bursitis.

However, if steroid use involves high doses and is prolonged (for a few months to several years), an increase in the number of side effects may occur.

To minimize the side effects of steroids, doctors follow these guidelines:

- Use steroids only when necessary.
- Monitor closely to detect the development of serious side effects.
- If possible, use steroid injections for problems in a specific area.
- Use the minimal dose required to gain control of the disease.
- Reduce the dose gradually as long as the disease remains under control.
- Monitor blood pressure often and treat if necessary.
- Recommend calcium supplements, vitamin D, and bone-building prescription medications to help maintain bone strength (this is done especially if steroids will be taken for a long period of time).
- Have your bone density checked every one to two years.

Steroids, as with other drugs, are not recommended for everyone. In general, people with the following conditions should not take steroids:

- Infection
- Uncontrolled diabetes
- Uncontrolled high blood pressure or congestive heart failure
- Peptic ulcer
- Osteoporosis (bone thinning)
- Glaucoma

The decision to prescribe steroids is always made on an individual basis. Your doctor will consider your age, your overall health, and other drugs you are taking. Your doctor also will make sure you understand the potential benefits and risks of steroids before you start taking them.[10]

Applications of Steroids in Endodontics: Endodontic pain is often associated with chronic inflammation, the presence of bacterial by-products, influx of immune cells and activation of the cytokine network and other inflammatory mediators. The chronicity of pulpal and periapical inflammation permits sprouting of nociceptor terminals and thus change the peripheral anatomy of the pain system. In humans, cortisol is the primary glucocorticoid that is continuously synthesized and secreted from the adrenal cortex. Glucocorticoids inhibit the inflammatory response by its effect on gene transcription that produces a decrease in the release of vasoactive and chemoattractive factors like bradykinin and certain cytokines that occur during periapical inflammation [11].

Glucocorticoids when given over a short course is unlikely to be harmful although it is contraindicated with patients that have systemic fungal infection, patients that have hypersensitivity to the drug, patients with ulcerative colitis, pyogenic infection, diverticulitis, peptic ulcer, renal insufficiency, hypertension, osteoporosis, pregnancy, diabetes mellitus, ocular herpes, acute psychosis and history of TB. Steroids have been used as intracanal medicaments, to control pain. Several studies also reported the use of steroids by systemic administration. Oral dexamethasone, intraligamentary, intrasseous and intramuscular administration of steroids have shown decrease in endodontic post treatment pain.

The studies show that they have the best efficacy and most appropriately used for those patients who present with moderate to severe pain and teeth with pulpal necrosis and associated radiolucencies (chronic inflammatory processes) than pain associated with irreversible pulpitis. Intraoral injection of 6-8mg of dexamethasone or 40mg of methylprednisolone OR oral dose of 48mg methlprednisolone/day for 3 days and 10-12mg dexamethasone/day for 3 days is suggested by the literature reviewed.

Antibiotics are not routinely recommended in conjuction with corticosteroids in the management of the otherwise healthy patient [12].

Up to 80% of endodontic patients who report with preoperative pain continue to experience some level of pain following the endodontic procedure. Various classes of drugs have been studied for the management of post-treatment endodontic pain. Since endodontic pain is often associated with chronic inflammation, the presence of bacterial by-products, influx of primed immune cells and activation of the cytokine network and other inflammatory mediators, pain may be reduced by administration of glucocorticoid steroids [13].

Other Medicinal use of Steroids: Steroids have several legitimate medical uses. Testicular cancer often requires the removal of the testes in men. After surgery, these men are prescribed oral steroids to replace the testosterone that their bodies are no longer able to make. This maintains their secondary sexual characteristics. Adolescent males with pituitary malfunction are treated with injectable steroids when they reach the appropriate age for puberty. Steroids given for four to six months in the proper dosing schedule cause the growth spurt and development of secondary sexual characteristics.

After certain kinds of surgery and cancer, the patient experiences loss of muscle tissue. Steroids are used in such cases, with exercise and diet, to build up muscle tissue. Steroids in high doses are given to transsexual women who wish to be permanently masculinized. This is not an officially approved medical use for steroids in the United States [14].

Steroids may one day be used as male oral contraceptives. However, their current negative image as abusable drugs has limited this research. Doses of steroids for medically approved uses range from 2.5 mg per day to 400 mg every 4 weeks. Usually, only a single steroid is taken at one time. Athletes take 8 to10 times the maximum recommended dose of each agent, and often take more than one type at a time. In typical dosing schedules, athletes are taking the equivalent of 20 to 2000 mg of testosterone per day, 2 to 200 times the normal dose [15].

For most legal prescription applications, steroid doses approximate the small amounts of steroids that would be produced naturally by the body. The right doses for different conditions are determined in drug company laboratories under controlled experimental conditions. Before a test dose of any new drug is given to a human volunteer, extensive studies are done on animals to find out how strong the drug is and how much to give.

By contrast, steroid abusers get their instructions by hearsay. Dosing directions are passed from one person to another without any evidence of effectiveness or adherence to medical prescribing standards.

CONCLUSION: The primary use of natural steroids in health care is to reduce inflammation and other disease symptoms. Steroid inhalers have an important role in reducing deaths from asthma, local steroid injections are useful in treating painful joints and ligaments. Steroid creams are used extensively to treat eczema and other inflammatory skin conditions. Steroids make the whole immune system less active, which can be very useful in illnesses where there is an immune component, a huge number. Steroids are the ultimate anti-inflammatory drugs.

Steroids is efficacious as an adjunct to but not a replacement for appropriate endodontic treatment in the lessening of endodontic post treatment pain.

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