

Safety of using **steroid hormones** as growth promoters



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By

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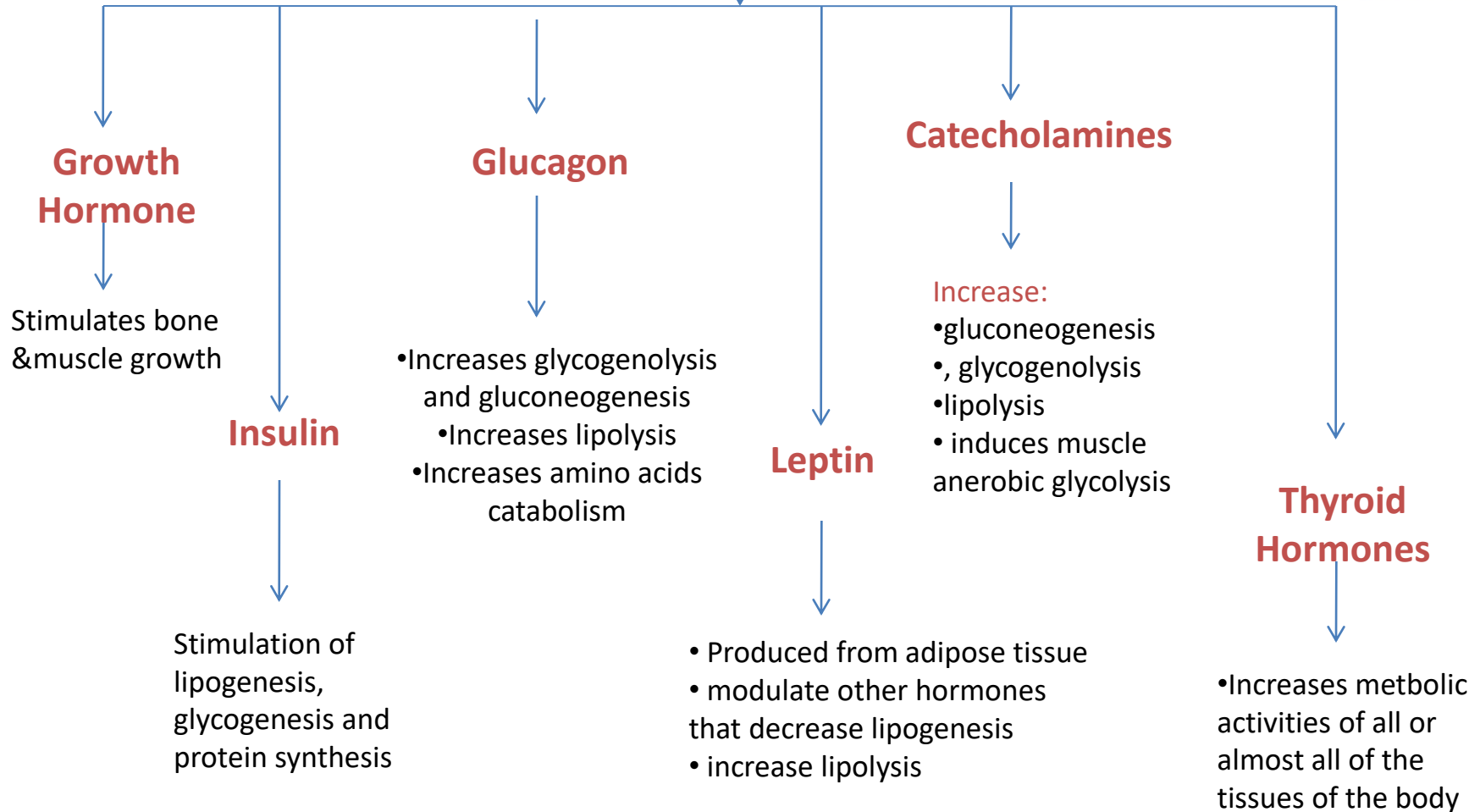




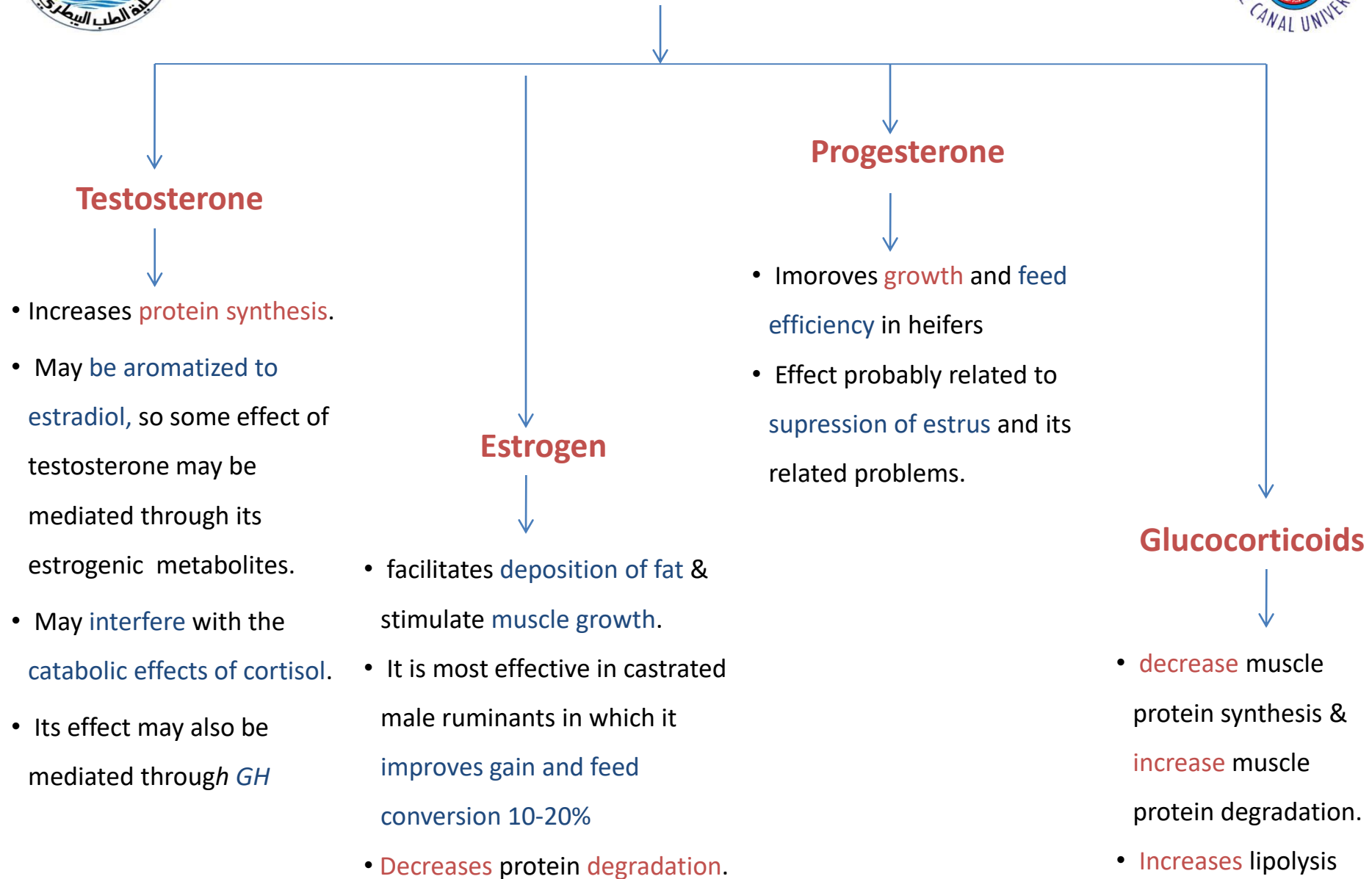
Hormones that affect growth



1. Non Steroid Hormones



2. Steroid Hormones



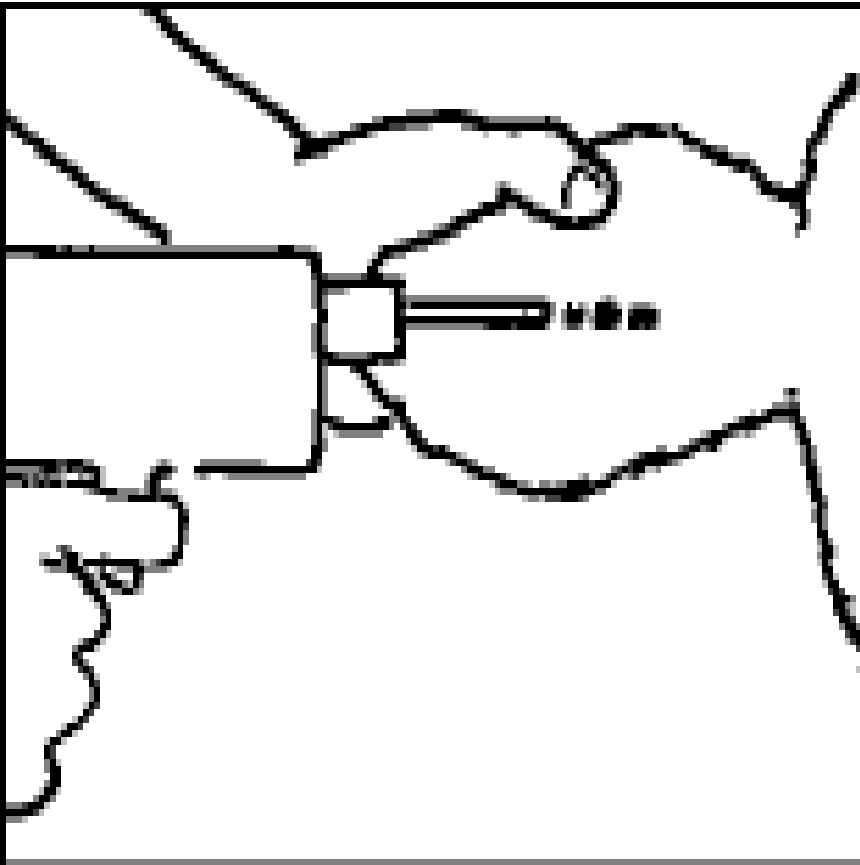
Hormones commonly used as growth promoters

- Six hormones are commonly used for growth purposes.
- Of the six hormones, **three** are naturally occurring and the other **three** are artificially produced.
- The naturally occurring hormones are:
 1. Oestradiol-17 β
 2. Progesterone,
 3. Testosterone),
- The artificially produced hormones are:
 1. Trenbolone acetate,
 2. Zeranol,
 3. Melengestrol acetate (MGA).



HORMONE PREPARATIONS USED IN ANIMAL PRODUCTION

- **1. Hormones of endogenous origin (natural hormones):**
- These comprise the “classical” steroid sex hormones, oestradiol-17 β , testosterone and progesterone.
- The two former are used either in the **free** form or as **esters**.
- **Esterification** generally causes **prolongation** of the **half-life** of the compounds in the body by **40 to 50%**.
- The natural hormones having **low bioavailability** when administered **orally**, owing to **rapid conjugation and metabolic transformation in the liver**.
- They are therefore administered by **subcutaneous implantation**.



2. Hormones of exogenous origin (synthetic hormones):

I. Of the synthetic oestrogens:

1. Zeranol – a synthetic, non-steroidal oestrogen, originally discovered in fungus-infected corn
2. Diethylstilboestrol (DES) and hexoestrol possess high biological activity and have been used most widely. They are active orally as well as by implantation.
3. Other orally active oestrogens include ethynyl-oestradiol, a more slowly metabolized derivative of the true hormone, with higher activity.

2. Hormones of exogenous origin (synthetic hormones):

II. The synthetic androgens: They comprise a large number of substances, most of which are steroids of these:

1. **Trenbolone acetate (TBA)** possesses **strong anabolic** properties and has received much attention during recent years, used **alone** or in **combination** with an **oestrogen**.
2. **Methyl-testosterone**: another anabolic steroid.

2. Hormones of exogenous origin (synthetic hormones):

III. Of synthetic gestagens: only one will be mentioned here:

1. Melengestrol acetate (MGA):

It stimulates growth in **heifers** but not in **steers**.

It can also be used for the suppression of oestrus.

2. Numerous other gestagens also exist, but at present **few other than progesterone and melengestrol acetate** are used to stimulate growth

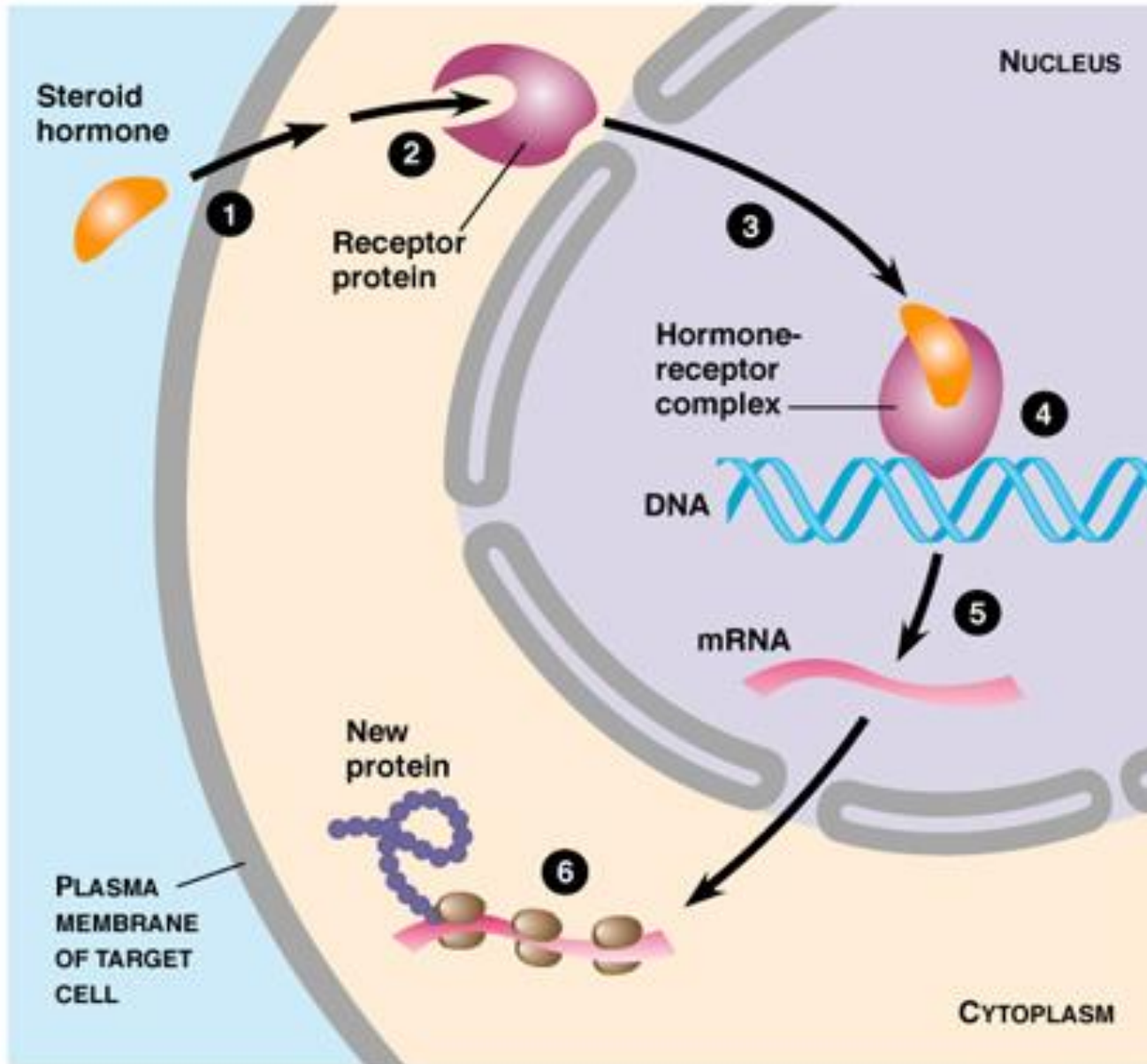
ECONOMIC IMPLICATIONS OF THE USE OF HORMONES IN ANIMAL PRODUCTION

- These anabolic agents are used for **increasing the rate of weight gain, improving the feed efficiency, storing protein and decreasing fatness** (Sawaya et al., 1998).
- In the production of meat for human consumption, a hormonally-induced **increase in growth rate** of the order of **10%** evidently has major economic implications.
- Some of the hormones that have become available recently appear on average to **increase** gain as well **as FCE** considerably beyond the **10%** level

6. MECHANISM OF ACTION OF HORMONES

- **No reliable explanation** of how the growth-promoting hormones act has yet been furnished.
- Some observations indicate a **direct** influence through stimulation of **protein synthesis** and an **indirect** influence through **changes in the balance of endogenous hormones**.

Mechanism of action of steroid hormones



Mechanism of action of hormones

1. Estrogen:

- The oestrogenic implants **increase protein deposition** by increasing the concentration of **growth hormone** (GH) secreted.
- It is the GH that stimulates the **anabolic** process of cell division, skeletal growth and protein synthesis (all growth promoting activity).
- At the same time the GH **increases the oxidation of fat** and **inhibits the transport of glucose to the body tissues**. This makes the **glucose and fatty acids** available as an **energy** source to the animal to **build muscle**.

Mechanism of action of hormones

2. androgens:

- Androgens competes with **glucocorticoids** for receptor sites on the muscle cell membrane.
- Since **glucocorticoids** have a catabolic effect on tissues, their displacement from muscle cells **would reduce catabolism**.
- **Testosterone** propionate is used in combination with **oestradiol benzoate**, specifically for heifers.

Mechanism of action of hormones

- **3. Progesterones**
- Progesterone is a female hormone that prepares the uterus for the **fertilised ovum** and helps to **maintain pregnancy**.
- Progesterone is used in '**combination with oestradiol benzoate**, specifically for use in **steers**.
- Hormones derived from **one sex**, when used in the **opposite sex**, produce **additional growth** in that animal.

Mechanism of action of hormones

4. Trenbolone acetate(synthetic testosterone,TBA):

- TBA increases the levels of **growth hormone** and/or of **insulin** in plasma. These hormones are known to **stimulate amino acid transport across the cell membrane**
- TBA **alone**, and even more when combined with **oestradiol-17 β** , causes a marked **decrease** in the concentration of total **thyroxine** in plasma of steers
- The **synthetic androgen trenbolone acetate** (TBA) has 8–10 times the anabolic activity of testosterone.
- Research has clearly shown TBA to promote growth **alone** at high growth rates.
- **TBA** is used in combination with **oestradiol benzoate** for use in **finishing** both steers and heifers.

5. **Melengestrol acetate (synthetic progesterone, MGA).**

MGA is 100 times more potent than progesterone in stimulating growth in feedlot heifers.

6. **Zeranol (synthetic estrogen)**

IT is a non steroidal compound which mimics the role of oestrogenic hormones.

Growth modifiers

- General types
 1. Antibiotic growth promoters
 2. Ionophores
 3. Implants
 4. β -adrenergic agonist
 5. melengestrol acetate (MGA)

Health hazards connected with the use of hormones in animal production

- Meat and meat products, which play an important role in human nutrition **should be safe and should not contain any factors or substances harmful for human health.**
- In recent years, **hormones** and hormone–like compounds have been frequently used in livestock production to obtain a **high yield performance in a shorter period of time.**
- However, **residues** that may occur in meat and meat products present risks to human health.
- As a result, **many countries restrict or prohibit** the use of anabolic compounds in livestock production, while **other countries allow its use.**

European and American point of view in this respect

- The **European Economic Community (EEC)** **banned** the use of anabolic compounds as growth accelerators in food animals.
- However, the **United States Food and Drug Administration (USFDA)** permitted the use of some hormones with **natural origins** (such as estradiol and testosterone) and some **synthetic hormones** such as trenbolone in animal husbandry.

The European Communities (EC) decision

- The European Communities (EC) prohibited the market and importation of meat and meat products that have **been treated with any of six hormones for growth purposes.**
- Of the six hormones, three are **naturally occurring** (17β , progesterone, testosterone), the other three are **artificially produced** (trenbolone, zeranol, MGA).

The reason for the European ban

- Human health and the consequences of using hormones have been linked with:
- increased risk of **endometrial** and **breast cancers** in women.
- **reproductive disorders in men.**
- They have also been shown to be **carcinogenic in** animal tests.
- **Progesterone** increases the incidence of **ovarian, uterine** and **mammary tumors** in experiments in laboratory animals.
- **Testosterone** may be **carcinogenic** in humans, having been linked with **prostatic** tumors in men.
- it has also been shown to be **carcinogenic** in **animal tests.**

The American point of view in this concern

- Regulatory authorities of:
- The U.S. Food and Drug Administration (**FDA**)
- Joint Food and Agriculture organization/World Health organization (**FAO/WHO**)
- Expert Committee on Food Additives (**ECFA**)

concluded that:

1. Regarding Natural Hormones:

- Estradiol-17 β , progesterone and testosterone are steroid hormones used in beef cattle growth promoting products.
- Each of these hormones **occurs naturally and is produced in significant quantities throughout the life time of every man, woman & child.**
- They are essential for the proper physiological functioning and maturation of all mammals.
- **Consumers are not at risk** from eating food from animals treated with these products because the **amount of added hormone** is **negligible** compared to the amount normally found in the edible tissues of untreated animals and the amount that is naturally produced by the consumer's own body.¹

- Therefore, no carcinogenic potential exists as a result of natural hormones from consumption of meat from either treated or untreated cattle.
- The committee **concluded that** the amount of estradiol-17 β , progesterone and testosterone ingested by eating beef from treated cattle would be **incapable of exerting a hormonal effect**, and, therefore, **incapable of exerting any toxic/carcinogenic effect in human subjects.**



Analysis of meat from cattle treated with hormones for growth promotion contain **15 000 times less estradiol** than the average **daily** amount produced by a **human male** and **several million times less** that the amount produced by a **pregnant woman**.

This is also the case for **progesterone** & **testosterone** Thus, the **FDA feels that the risk is negligible compared to the consumer's own daily production**.



FDA/CVM Regulatory Decisions concerning synthetic hormones

1. Trenbolone Acetate (TBA):

- After extensive **dose-response carcinogenetic studies** in mice and rats, the Cancer Assessment Committee of the CVM concluded that **Trenbolone Acetate** (TBA) is not a carcinogenic.
- After extensive studies, the CVM also concluded that TBA and both the 17α -OH-trenbolone and 17β -OH **trenbolone metabolites** are **not mutagenic**.^{9, 10}

2. Zeranol

- Human food safety documented that **zeranol** is neither a carcinogen nor mutagen.
- Using a gas chromatographic method with a sensitivity limit of 20 ppb, **no residues of zeranol** could be detected in edible tissue from cattle slaughtered **65 days following implantation**.
- In another study, tritiated zeranol was implanted in cattle as part of 36-mg doses. **Skeletal muscle obtained 10, 30 and 50 days** following implantation contained **no detectable residual activity** (99).
- *Consequently **CFDA/CVM concluded** that meat and meat products derived from cattle implanted **with zeranol are safe for human consumption**.*

3. Melengestrol Acetate(MGA):

- The Fifty-fourth Report of JECFA (2001) concluded that melengestrol acetate(MGA) **is neither carcinogenic nor genotoxic.**



- The **FDA** has concluded that it is **unnecessary** to monitor these hormones in meat because these levels **could not reach a concentration deemed to be unsafe even in cases of misuse.**
- The FDA has also recognized the impossibility of banning these agents because analytical methodologies cannot distinguish between naturally-occurring hormones and hormones found in meat as a consequence of administration for growth promotion purposes.



JUST WANTED TO SAY



THANKS!



**RESPECT
MY
HORMONES**

Paylean™ - Ractopamine

- Small compound;
- Partitions energy from fat growth to lean growth;
- Increases protein accretion and muscle growth;
- Increases muscle fiber diameter.

What is Ractopamine?

- β agonist;
- not a hormone;
- not a steroid;
- not “biotechnology.”

Outline of Presentation

- Codex Alimentarius:
 - What is it? What does it do?
 - Importance for national legislation
- International Health Regulations (2005):
 - Background, overview, scope
 - Key elements
 - Importance of intersectoral collaboration
- Legislative assessment and revision:
 - Lessons learned and practical suggestions

Codex Alimentarius Commission

- what is it? -

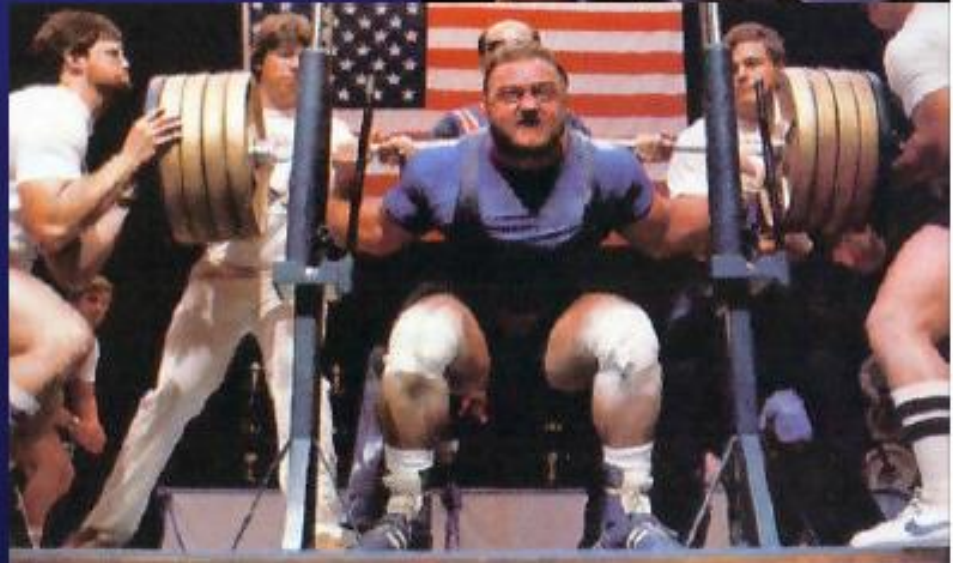
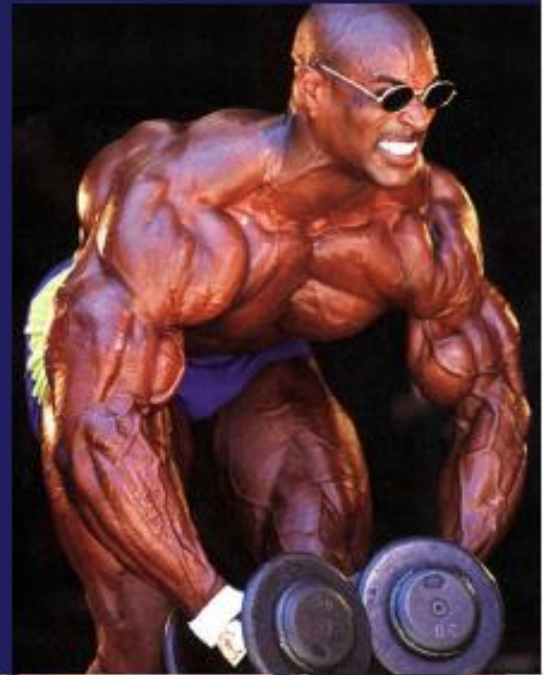
- Codex Alimentarius Commission (CAC) is an intergovernmental body operating within the United Nations
- Joint initiative of FAO and WHO (since 1963)
 - FAO/WHO Food Standards Programme
- 180 member governments, including the European Community as a member organization
- Approximately 20 technical committees
- Product is Codex Alimentarius (Latin for "food code")

FAO/WHO Guidelines for strengthening national food control systems (2003)

- **ANNEX 6 – Guidelines for Developing a National Food Law**
- A set of guiding principles as a general approach to the drafting of food legislation
- Applicable to different legal systems
- Complement an in-depth analysis of the legal and institutional framework that govern food production, import, export, distribution, handling and sale in a particular country
- Prompt countries to take full advantage of Codex standards and food safety & quality lessons learned in other countries

Myogenesis

- **Myo = Muscle**
- **Genesis = Coming to being**
- **Two types of growth**
 - **Hypertrophy – increase in cell size**
 - **Hyperplasia – increase in cell number**

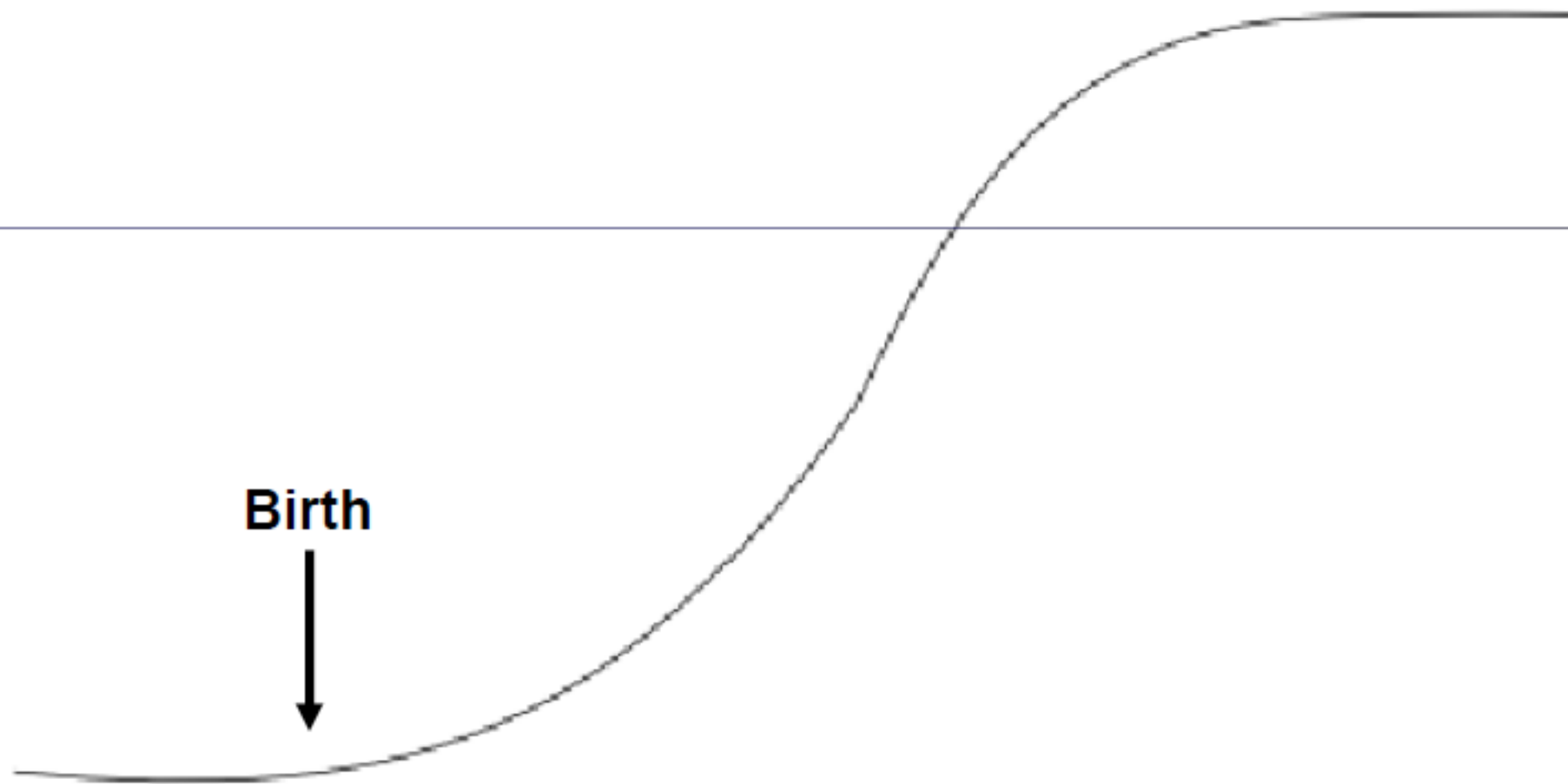


How do I get from here to there?



Growth

Birth



Growth

- **Determinate Growth**
 - Mammals
 - Grow to a given size (mature size)
- **Indeterminate Growth**
 - Fish
 - No predetermined size
 - Will grow to available nutrients and environment
 - Can create new muscle fibers after hatching



Postnatal Growth

- **Phase III**
 - 80 to 90% of growth complete
 - 80 to 90% of muscle is deposited
 - Rapid accumulation of fat
- **Phase IV**
 - 90 to 95% of additional growth is fat
 - 5 to 10% of gain is muscle

Postnatal Growth

- **Phase I**
 - 15 to 20% of total growth
 - Slow growth of all tissues
 - Organs > Bone > Muscle
- **Phase II**
 - ~75% of total growth
 - Organ & bone growth complete
 - Muscle hitting maximal growth
 - Fat accumulates slowly

Protein Synthesis and Degradation

- **Protein Turnover = process of building protein, the replacing it with newly synthesized protein**
- **Protein Accretion = more synthesis than degradation**
- **Atrophy = more degradation than synthesis**



What else affects muscle growth?

- Genetics
- Nutrition
- Hormones
 - Sex
 - Age
- Growth Promotants



Hormones

- **Sex hormones**
 - **Testosterone (other androgens such as androstenone and adrenal androgens)**
 - Increases bone growth
 - Shortens G1 phase
 - Increase protein synthesis
 - **Estrogen**
 - Facilitates fat deposition
 - Stimulate muscle growth
 - Very anabolic in ruminants
- **Growth Hormone or Somatotropin**
 - Major action is to the production of Insulin – like Growth Factor I
 - Increase protein synthesis and decrease protein degradation
 - Increases lipolysis; mobilizes fatty acid from adipocytes

Antibiotic growth promoters

- Any medicine that destroys or inhibits bacteria **and** is administered at a low, subtherapeutic dose
- Main antibiotics added to cattle feed
 - Chlortetracycline
 - Oxytetracycline
 - Tylosin
- 3 to 5 % improvement in gain and FE
- No withdraw if fed at subtherapeutic dose

Growth Promotants

- Increase muscle cell size
- Beef Implants
 - Trenbolone Acetate
 - Estradiols
- Pigs and Cattle
 - Ractopamine hydrochloride
 - Paylean and Optaflex
- Cimaterol, Isoproterenol, and Clenbuteral (illegal)
- PST (Porcine Somatotropin; not approved)

Hormones

- **Insulin**
 - Increases storage of:
 - Glucose = Glycogen
 - Fatty Acids = Triglyceride
 - Amino Acid = protein
- **Leptin**
 - Decrease food intake
 - Increase energy expenditure
 - Decrease fat mass



Ne Dept Ag

Cattle Implants

- No withdrawal times
- Effect lasts:
- Ralgro 80 days
- Synovex S 80-90 days
- Synovex X 90 days
- Revalor 90 days

Pay-Lean

- Recommended use 4.5 to 9 grams per ton
- Problem comes from top dressing over use



Some of the residues

❖ **Drugs /antibiotic**

Antibiotics, coccidiostat, Anthelmentics, Acaricides,
Topical antiseptics

❖ **Insecticide**

Chlorinated Hydrocarbons & organophosphates

❖ **Metals**

Lead, arsenic, mercury, cadmium etc,...

❖ **Hormones**

Safety compounds-
Estradiol,
Progesterone,
Testosterone.

Non safety compounds-
Oxytocin,
Thyroid

Types of Food Contamination

- Biological
- Chemical
- Physical

FOOD SAFETY :-

A suitable edible product which when consumed orally either by a human or an animal does not cause any health risks (to consumer

RESIDUES:-

These substances having a pharmacological actions of their metabolites and of other substances transmitted to animal products and which are likely to be harmful to human health.

Some of the residues

❖ **Growth Promoters**

Arsenicals , Antibiotics, Clenbuterol

❖ **Natural toxins**

Aflatoxin, Ochratoxin, Etc

❖ **Environmental contaminants**

Herbicide, Fungicide.

❖ **Preservatives :**

Sulphur, Dioxide, Sodium, Potassium ,Nitrite

❖ **Other substances:**

Fluoride

Intensive Animal Production

- From Animal husbandry To Meat Production
 - Gestation crates, Early weaning, debeaking, Growth promoting synthetic hormones & feed additives
- From Geographically dispersed to highly concentrated
- From Pasture-based to Confinement based

