The Thyroid "Transplant"

Mirrors natural thyroxine so closely, TSH levels indistinguishable from normal

Provides dose-to-dose precision, to ensure consistent thyroxine delivery

Offers the widest range of dosage strengths, to meet each patient's precise thyroxine requirements

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Please see Brief Summary of Prescribing Information following adjoining page.

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Closest you can get to normal thyroid function

SYNTHROID®
(Levothyroxine Sodium) Tablets, USP

- 25 mcg
- 50 mcg
- 75 mcg
- 88 mcg
- 100 mcg
- 112 mcg
- 125 mcg
- 150 mcg
- 175 mcg
- 200 mcg
- 300 mcg
SYNTHROID®
(Levothyroxine Sodium, USP)
Precise
Affordable
Available

DESCRIPTION. SYNTHROID® (Levothyroxine Sodium, USP) Tablets and Injection contain synthetic crystalline L-3,3',5,5'-tetraiodothyronine sodium salt (levothyroxine (T4) sodium). SYNTHROID® is similar to that produced in the human thyroid gland. T4 conjugates four iodine atoms and is formed by the coupling of two molecules of diiodotyrosine (DIT) with a tyrosine residue of thyroglobulin. SYNTHROID® has an empirical formula of C15H11I4N3O4S, molecular weight of 788.82 (anhydrous).

INDICATIONS AND USAGE. SYNTHROID is indicated 1. As replacement or supplemental therapy in patients with hypothyroidism of any etiology, including but not limited to: 1. Primary (congenital or iatrogenic) thyroid insufficiency; 2. Secondary (pituitary thyroid hormone deficiency); 3. Tertiary (dysfunction of the hypothalamic-pituitary-thyroid axis); 4. Congenital hypothyroidism; 5. Hyperthyroidism; 6. Thyroid gland autonomy.

CONTRAINDICATIONS: Thyroid hormone preparations are generally contraindicated in patients with hyperthyroidism or thyroid gland autonomy.

ADVERSE REACTIONS: Adverse reactions other than those indicative of hyperthyroidism are infrequent. Serious adverse reactions and does not have known tumorigenic potential. While caution should be exercised when thyroid is started. If a patient is truly hypothyroid, it is likely that a reduction in anticoagulant dosage will be necessary. If the special preparation appears to be necessary and anticoagulants are also being given, compensatory increases in clotting factor synthesis are impaired. Patients should be initiated immediately upon diagnosis, and maintained for life, unless transient hypothyroidism is suspected; otherwise, excessive doses of thyroid hormone may produce hyperthyroidism.

WARNINGS. Drugs with thyroid hormone activity, alone or together with other therapeutic agents, have been used with the treatment of obesity. In euthyroid patients, doses within the range of daily hormone requirements are effective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of hyperthyroidism, particularly when given in association with sympathomimetics such as these for their anesthetic effects.

The use of thyroid hormones in the therapy of obesity, alone or combined with other drugs, is unverified and has been attempted occasionally. The use of thyroid hormones in obesity is not recommended.

PRECAUTIONS. General. Thyroid hormones, should be used with great caution in patients who have a history of cardiovascular disease. In these patients, therapy should be initiated with low doses (e.g., 25-50 mcg levothyroxine T4). In patients who are thyrotoxic, the symptom and signs indicative of cardiovascular disease; thyroid hormone dosage should be reduced. Thyroid hormone therapy in patients with concurrent diabetes mellitus or insulin or oral antidiabetic agents is well tolerated. Tests of the severity of these symptoms are necessary in all patients with cardiovascular disease. Thyroid hormone therapy in patients with coronary artery disease, the elderly, who have a greater likelihood of occult cardiac disease. Therapy in these patients, should be initiated with low doses (e.g., 25-50 mcg levothyroxine T4). In patients who are thyrotoxic, the symptom and signs indicative of cardiovascular disease; thyroid hormone dosage should be reduced. Thyroid hormone therapy in patients with concurrent diabetes mellitus or insulin or oral antidiabetic agents is well tolerated. Tests of the severity of these symptoms are necessary in all patients with cardiovascular disease.

Information for Patients: For full prescribing information, see package circular.

Laboratory Tests. Treatment of patients with thyroid hormones requires the periodic assessment of thyroid status by measurement of serum pituitary tests, by full clinical evaluation or both. The 2 T4 suppression test can be used to test the effectiveness of any thyroid hormone-bearing in the relative level of the patient's pituitary to the normal. Normal serum T4 levels can be used to test the effectiveness of thyroid hormone therapy. When the total serum T4 is low but TSH is normal, a test specific to assess unbound (free) T4 levels is warranted. Specific measurements of T4 and T3 by competitive protein binding or radioimmunoassay are not influenced by blood levels of organic or inorganic iodine and have essentially replaced direct tests of thyroid hormone measurements.

Drug Interactions: Thyroid hormones appear to be increased in concentration of vitamin K-dependent clotting factors. Oral anticoagulants. There also being less significant increases in clotting factor synthesis, are also increased. Patients stabilized on daily anticoagulant therapy who are being treated with thyroid hormone therapy may need to increase their oral anticoagulant dosage. The effectiveness of any thyroid hormone-bearing in the relative level of the patient's pituitary to the normal. Normal serum T4 levels can be used to test the effectiveness of thyroid hormone therapy. When the total serum T4 is low but TSH is normal, a test specific to assess unbound (free) T4 levels is warranted. Specific measurements of T4 and T3 by competitive protein binding or radioimmunoassay are not influenced by blood levels of organic or inorganic iodine and have essentially replaced direct tests of thyroid hormone measurements.

Pregnancy: SYNTHROID® (Levothyroxine Sodium, USP) Tablets are available for the treatment of obesity. In euthyroid patients, doses within the range of daily hormone requirements are effective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of hyperthyroidism, particularly when given in association with sympathomimetics such as these for their anesthetic effects.

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- A complete thyroid diagnostic range on one system based on sensitive chemiluminescence method
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  BeriLux® T3, BeriLux® FT3
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AWP Comparison of Levoxine with Synthroid and Levotroid

Levoxine is the only brand name levothyroxine packaged in 100's and 1000's, unit dose and samples in all eleven strengths.

*Synthroid* is a registered trademark of Boots Pharmaceuticals, Inc.; *Levothroid* is a registered trademark of Forest Pharmaceuticals, Inc.
crystalline levothyroxine sodium (L-thyroxine). The principal effect of thyroid hormones is to increase the metabolic rate.

3,5-diiodomonosodium salt, hydrate. The molecular formula is

\[
\text{C}_15\text{H}_{11}\text{I}_{2}\text{O}_{4}\text{Na}_2\cdot\text{H}_2\text{O}
\]

absorption cannot be distinguished from T4 that is secreted endogenously, it is a product hormone secreted by the normal thyroid gland. Chemically, L-thyroxine (L-thyroxine) is chemically identical to T4, the free thyroid index and thyroid stimulating hormones (TSH) blood levels.

Drug Interactions: In patients with diabetes mellitus, addition of thyroid hormone therapy may cause an increase in the required dosage of oral antidiabetic agents. Therefore, patients with diabetes mellitus should be observed closely for possible changes in antidiabetic drug dosage requirements.

Patients stabilized on oral anticoagulants who are found to require thyroid replacement therapy should be watched very closely when therapy is started. For patients not on anticoagulant therapy, a reduction in anticoagulant dosage will be required.

Drug/Laboratory Test Interactions: The following drugs or moieties are known to interfere with laboratory test procedures in patients taking thyroid hormone preparations. Anticoagulants, corticosteroids, estrogens, oral contraceptives containing estrogens, iron-containing preparations, and the numerous preparations containing salicylates.

INDICATIONS AND USAGE: LEVOXINE (L-thyroxine) tablets are indicated as replacement therapy for diminished or absent thyroid function (e.g., cretinism, myxedema, non-toxic goiter or hypothyroidism generally, including the hypothyroid state in children, in pregnancy and in the elderly) resulting in the interpretation of T4 and T3 values. In such cases, the unbound fraction of thyroid hormones has no effect on the measurement of hormone binding pre-albumin (TBPA) is inhibited by salicylates.

CONTRAINDICATIONS: L-thyroxine therapy is contraindicated in patients with a non-functioning thyroid gland who is receiving thyroid hormone therapy or in patients who have had a thyroidectomy. Estrogens tend to increase serum thyroxine-binding globulin (TBG). In patients with untreated hypothyroidism, 0.9 mg of L-thyroxine may be administered intravenously over a 10 minute period or orally, 80 to 160 mg/day, especially when no contraindications exist for its use.

ADVERSE REACTIONS: Adverse reactions are due to overdosage and are those of induced hyperthyroidism. The most common signs and symptoms of thyroid hormone therapy are as follows:

1. Changes in TBS concentration should be taken into consideration when interpreting T4 and T3 values. In such cases, the unbound fraction of thyroid binding globulin (TBG) can be estimated. Estrogens tend to increase serum thyroxine-binding globulin (TBG). In patients with untreated hypothyroidism, 0.9 mg of L-thyroxine may be administered intravenously over a 10 minute period or orally, 80 to 160 mg/day, especially when no contraindications exist for its use.

DOSAGE AND ADMINISTRATION: The goal of therapy should be the restoration of euthyroidism as judged by clinical response and confirmed by appropriate laboratory tests such as serum proteinuria (T4), serum immunoglobulin (T3), thyroxine index and stimulating hormone levels. The appropriate dosage regimen is begun. The most common signs and symptoms of thyroid hormone overdosage are those of induced hyperthyroidism. The most common signs and symptoms of thyroid hormone therapy are as follows:

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DOSAGE FORMS AVAILABLE: LEVOXINE (L-thyroxine) tablets are supplied as oral, color coded, potency marked tablets in 11 strengths: 25 meg (0.025 mg)-orange, 50 meg (0.05 mg)-white, 75 meg (0.075 mg)-purple, 88 meg (0.088 mg)-pink, 125 meg (0.125 mg)-brown, 150 meg (0.15 mg)-blue, 175 meg (0.175 mg)-blue, 200 meg (0.2 mg)-blue and 300 meg (0.3 mg)-green, in bottles of 100 and 1000, and unit dose in cartons of 100 (10 strips of 10 tablets).

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The JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM publishes endocrine and metabolic studies related to human and primate physiology and disease. ENDOCRINOLOGY publishes nonprimate biochemical and physiological studies, although work on material of primate origin is not excluded. MOLECULAR ENDOCRINOLOGY publishes studies of the effects of hormones and related substances on the molecular biology and genetic regulation of nonprimate and primate cells. ENDOCRINE REVIEWS publishes quarterly and features in-depth review articles on both experimental and clinical endocrinology. Authors are invited to consult with the Editors concerning the most appropriate journal to which to submit their manuscripts.

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The JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM publishes endocrine and metabolic studies related to human and primate physiology, biochemistry and disease. ENDOCRINOLOGY publishes nonprimate biochemical and physiological studies, although work on material of primate origin is not excluded. MOLECULAR ENDOCRINOLOGY publishes studies of the effects of hormones and related substances on the molecular biology and genetic regulation of nonprimate and primate cells. Authors are invited to consult with the Editors concerning the most appropriate journal to which to submit their manuscripts.

GENERAL INFORMATION

Manuscripts are of three types: Original Studies, Rapid Communications, and Comments. Original Studies should be original investigative reports. Rapid Communications must be no longer than three journal pages and should contain important new observations of sufficient significance to endocrinologists in general to warrant rapid publication; see Appendix G. Comments are brief manuscripts reporting data that are preliminary, negative or confirmatory. The usual form for manuscripts should be followed.

A manuscript that is not returned to the Editorial Office within six months after being sent to the author(s) for revision will be treated as a new manuscript.

A rejected manuscript that is resubmitted will be treated as a new manuscript.

ETHICAL CONSIDERATIONS

The foremost obligation of an author is to present a clear, honest, accurate, and complete account of the research performed. Each manuscript should describe a complete study or a completed phase of an extended study. Fragmentation of reports should be avoided. When some of the results are to appear in another journal, or in publications of congresses, symposia, workshops, etc, details should be supplied to the editor, and a copy of the other paper(s) submitted.

The author also has an obligation to: 1) Describe the work in sufficient detail to allow others to repeat the work; 2) Include all relevant data, including those which may not support the hypothesis being tested; 3) Cite those publications which have a direct bearing on the novelty and interpretation of the results; 4) Make any clones, whether of cells or genes, published in this Journal available to interested investigators.

Only individuals who made significant contributions to the intellectual and procedural aspects of the study should be listed as authors. An author should have participated in the conception and planning of the work, the interpretation of the results, and the writing of the paper. An acknowledgment accompanying the paper is appropriate recognition for others who contributed to a lesser extent. The signature of each author on the Affirmation of Originality and Copyright Release form which must be submitted with the manuscript indicates that the author approved the final version of the manuscript and that he is prepared to take public responsibility for the work.

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SPECIFICATIONS

I. Manuscript Style


Manuscripts should be clearly and concisely written. The manuscript should be carefully scrutinized for errors before it is submitted. Correctness of spelling, grammar, and typing is the responsibility of the author. Foreign contributors, whose language is not English, should enlist the help of colleagues who are proficient in scientific English. Laboratory slang, clinical jargon, and colloquialisms must be avoided.

Manuscripts must be submitted as double-spaced typewritten copy with wide margins on 216 × 279 mm (8 1/2 × 11) inch paper and must be in Quadruplicate; this requirement applies to all tables and photocopies of figures, as well as to text.

The title page with the authors' names and institution, tables, references, footnotes, legends, and bibliography must be on separate pages.

II. Form of Manuscript

1. Title: This should be a concise statement of the article's major contents. It should provide sufficient information to allow the reader to judge the relevance of a paper to his interest.

   An abbreviated title of not more than 40 letters and spaces must be provided for page headings.

2. Abstract: This should not exceed 200 words in length. It should describe briefly in complete sentences the purpose of the study, the methods utilized, the results obtained, and the principal conclusions. The abstract must be easily understood without recourse to the text or list of references. Avoid nonstandard abbreviations, unfamiliar terms, symbols, or acronyms not easily understood by the general reader.

3. Introduction: The introduction orients the reader in respect to the state of knowledge in the area under investigation. It assumes that the reader has a basic knowledge of clinical endocrinology and metabolism. It should cite recent important work by others.

4. Experimental Subjects: It is assumed that all clinical investigation described in submitted manuscripts was conducted in accordance with the guidelines proposed in The Declaration of Helsinki (see Appendix A). The study populations should be described in detail. In many studies details of age, race, and sex are important. In experiments involving any significant risk or discomfort to subjects, it should be documented that informed consent was obtained from the subjects and that the investigations had been approved by an institutional human research committee.

   In text, tables, and figures subjects must be identified by number or letter rather than by initials or names.

   Photographs of patients' faces should be included only if scientifically relevant. Authors should obtain written consent from the patient for use of such photographs.

5. Experimental Animals. It is assumed that all animal experimentation described in submitted manuscripts was conducted in accord with the highest standards of humane animal care, as outlined in Appendix B. The manuscript should include a statement that any animal studies were conducted in accord with the principles and procedures outlined in this Appendix.

6. Materials and Methods: These should be described and referenced in sufficient detail so that other workers can repeat the work. The source of hormones, unusual chemicals and reagents, and special pieces of apparatus should be stated. For modified methods only the modifications need be described.

7. Results: The experimental data should be presented briefly in text, tables, or figures, but the authors should avoid redundant methods of presentation.

   Figures should be prepared in such a manner as to minimize the
space required for their reproduction. Several figures should be combined into one composite figure whenever possible.

Lettering on figures should be as large as possible in order to permit maximal reduction in size. In photographs show only a close-up of the region of interest. Tabular material may be inserted into the "blank" area of a figure. As a rule 13 x 18 cm (5 x 7 inch) prints are preferred.

Most graphs must be of professional quality and submitted only as sharp photographs on glossy paper. These and other photographs should be unmounted and trimmed to exclude all but the essential areas. Each figure must be numbered on the back, and the top must be indicated. Submit only one set of unmounted glossy figures. Each copy of the manuscript must have a set of clear photocopies of clearly numbered figures appended—one figure to a page. When photomicrographs are included, submit glossy prints (not photocopies) with each copy of the manuscript.

By the author's request and at his expense, half-tone such as photo- or electron micrographs may be custom printed on special paper from engravings approved by the author. Prices will be quoted on request.

Tables must be submitted in the form of typewritten copy. Each table must have a concise heading and be constructed as simply as possible; it must be intelligible without reference to the text. Not more than four vertical rows should be planned for a small table (a table designed to occupy the width of one column) and not more than eight to ten rows for a large table (one designed to occupy both columns of a page).

Care should be taken to minimize redundant or repetitious entries in a table. For instance, rather than stating "P < 0.05" for each of 20 comparisons within a table, it is sufficient to use an asterisk or other special symbol to denote specified probability levels defined in a footnote to the table.

8. Discussion: The discussion should be focused on the interpretation and significance of the findings, and brief, objective comments describing their relation to other work in the field. Repetition of material in the Introduction and the experimental findings should be avoided. Unsubstantiated speculations and plans for future study must not be included.

9. References: References to the literature should be cited in numerical order (in parentheses) in the text. There must be only one reference to a number.

The number of references cited should be kept to a reasonable minimum; to this end, appropriate recent reviews should be cited whenever possible. The citation of unpublished observations, of personal communication, or of manuscripts which have been prepared or submitted for publication is not permitted in the bibliography. Such citations should be inserted at appropriate places in the text, in parentheses and without serial number, or be presented in footnotes.

Examples of the reference style that should be used are given below. Further examples will be found in the articles describing the Uniform Requirements (Ann Intern Med. 1988;108:258-65, Br Med J. 1985;290:101-5). The title of journals should be abbreviated according to the style used in Index Medicus.

Journal articles and abstracts: List all authors when six or fewer; when seven or more, list only the first three and add et al.


study, data regarding performance characteristics should be included.

2. Pulse Analysis: Data from studies of pulsatile hormone secretion should be analyzed using a validated, objective pulse detection algorithm. The algorithm used should require that false-positive rates of pulse detection be defined in relation to the measurement error of the data set being analyzed, and the methods used to determine the measurement error should be described. The author(s) also should describe the methods used: 1) to deal with missing or undetectable values, 2) to determine peak frequency, interpeak interval, and pulse amplitude, and 3) for statistical comparisons of peak parameters.

3. Data Analysis: It is the author's responsibility to document that the results are reproducible and that the differences found are not due to random variation. Appropriate statistical methods should be used to test the significance of differences in results. The term “significant” should not be used unless statistical analysis was performed, and the probability value used to identify significance (e.g. \( P < 0.05 \)) should be specified.

When several \( t \) tests are employed, authors should be aware that nominal probability levels no longer apply. Accordingly, the multiple \( t \) test, multiple range test, or similar techniques to permit simultaneous comparisons should be employed. Also, in lieu of use of several \( t \) tests, it is often more appropriate to utilize an analysis of variance (ANOVA) to permit pooling of data, increase the number of degrees of freedom, and improve reliability of results. Authors should use appropriate nonparametric tests when the data depart substantially from a normal distribution.

Analysis of variance tables should not be inserted in manuscripts. \( F \) values with the degrees of freedom as subscripts together with the \( P \) values are sufficient. In presenting results of linear regression analyses, it is desirable to show 95% confidence limits.

IV. Proof and Reprints

Proofs and a reprint order form are sent to the first author unless the Editorial Office is advised otherwise.

The author should designate by footnote on the title page of the manuscript the name and address of the person to whom reprint requests should be directed.

V. Page and Other Charges

There will be a charge of $35 per printed page in the journal. There will be additional charges for color illustrations, as well as excessive or other unusual illustrative material.

In extraordinary cases, on appeal by the author, the Publications Committee may waive the page or other charges.

APPENDIX A

Declaration of Helsinki: Recommendations for Conduct of Clinical Research

Introduction

It is the same mission of doctors to safeguard the health of people. Their knowledge and conscience are dedicated to the fulfillment of this mission. The Declaration of Geneva of The World Medical Association binds the doctor with the words: “The health of my patient will be my first consideration” and the International Code of Medical Ethics which declares that “Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest.” Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, The World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and the clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical person.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in the doctor’s judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

2. If at all possible, consistent with patient psychology, the doctor should obtain the patient’s freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

3a. Clinical research on a human being cannot be undertaken without the patient’s consent after being informed; if the person is legally incompetent the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully the power of choice.

3c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

4a. If at all possible, consistent with patient psychology, the doctor should obtain the patient’s freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

4b. The investigator must respect the right of each individual to safeguard his/her personal integrity, especially if the subject is in a dependent relationship to the investigator.

4c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

4d. The investigator or the investigating team should discontinue the research if in their judgment, it may, if continued, be harmful to the individual.

III. Nontherapeutic Clinical Research

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken without the patient’s consent after being informed; if the person is legally incompetent the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully the power of choice.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

13A
INSTRUCTIONS TO AUTHORS

APPENDIX B

Guidelines for The Care and Use of Experimental Animals

The Society requires that all studies involving the use of animals published in its journals be conducted in accordance with the highest standards of humane care. The appropriateness of the experimental procedures, as well as the species and required number of animals used, must be considered in the design of any study. All research animals must be acquired and used in compliance with federal, state and local laws and institutional regulations. In particular, the Society recommends that animals be maintained in accordance with the NIH Guide for the Care and Use of Laboratory Animals.

Research animals must receive appropriate tranquilizers, analgesics, anesthetics and care to minimize pain and discomfort during preoperative, operative, and postoperative procedures. The choice and use of drugs must be made in accordance with the NIH Guide. Where the use of anesthetics would negate the results of the experiment, the protocol must be clearly justified and approved by the Committee on Animal Care and Use of the local institution and according to accepted veterinary medical practice. The health of the animals must be properly monitored. If either the study or the condition of the animals requires that they be killed, it shall be done in a humane manner.

APPENDIX C

Abbreviations And Symbols

(Note that periods are omitted in abbreviations)

- absorbance (A = log 1/T)
- adenine diphosphate
- adenosine diphosphate
- bovine serum albumin
- correlation coefficient
- counts per minute
- 3',5'-cyclic AMP
- degrees Celsius
- deoxyribonucleic acid
- diphosphopyridine nucleotide
- diphosphopyridine nucleotide, reduced form of
- disintegrations per minute
- extinction (molar extinction coefficient)
- gram
- kilograms
- micrograms
- nanograms
- plasma renin activity
- probability
- radioimmunassay
- radioreceptor assay
- second
- specific activity
- standard deviation
- standard error
- subcutaneous
- Student's "t" test
- thyroxine
- T3
- T4
- triiodothyronine
- TSH-releasing hormone
- thyroid-stimulating autoantibodies
- US
- weight
- weight/volume (concentration)
- year
- osmol/kg
- volume
- wt
- wt/vol
- year
- m
- mL
- mmol/L
- mL
- mol wt
- mol
- per cent
- %

APPENDIX D

Abbreviations for Polypeptide Hormones

1. Standard abbreviations (Can be used without definition, but they should be spelled out in the title.)

- ACTH-releasing hormone
- Adrenocorticotropic hormone
- Atrial natriuretic hormone
- Follicle-stimulating hormone
- Gonadotropin-releasing hormone
- Growth hormone
- Growth hormone
- Chlorionic gonadotropin
- Luteinizing hormone
- Melanocyte-stimulating hormone
- Parathyroid hormone
- Proopiomelanocortin
- Prolactin
- Thyrotropin
- Thyroid-stimulating hormone
- Thyroid-stimulating autoantibodies
- factor I or II
- Lyase vasopressin
- Oxytocin

3. Species designation is by lower case letter preceding the hormone abbreviation. These should not be used when referring to human hormones unless species ambiguity could exist.

Examples

- bovine GH
- human GH
- ovine GH
- porcine GH
- rat GH
APPENDIX E

Nomenclature of Steroids

1. Steroids should be named, whenever possible, according to the rules of the International Union of Pure and Applied Chemistry (IUPAC) [Biochemistry (Wash) 8: 227, 1969].

2. Any substituted steroid should be named in such a manner that one and only one type of functional group is used as a suffix and this group should be the principal functional group as defined in Chemical Abstracts 54, Subject Index, p. 5R, Item 2, 1960.

3. All other functional groups should be stated as prefixes in the order prescribed by Chemical Abstracts Inc., Item 7.

4. If the first letter of the suffix designating the principal functional group is a vowel, the terminal "e" of the name of the hydrocarbon should be dropped.

5. The following trivial names for steroids may be used without a footnote definition. Cholesterol (cholester-5-ene-38-ol), estrone (3-hydroxyestr-1,3,5(10)-triene-17-one), 17β-estradiol (estra-1,3,5(10)-triene-3,17β-diol), estriol (estra-1,3,5(10)-triene-3,16α,17β-triol), aldosterone (11β,21-dihydroxy-18-oxopregn-4-ene-3,20-dione), androsterone (5α-hydroxy-5α-androstan-17-one), etiocholanolone (5α-hydroxy-5α-androstan-17-one), dehydroepiandrosterone (5β-hydroxy-5α-androstan-17-one), testosterone (17β-hydroxyandrost-4-en-3-one), androstenedione (androst-4-en-3,17-dione), progesterone (pregn-4-en-3,20-dione), corticosterone (11β,17α-dihydroxyprogren-4-ene-3,20-dione), deoxycorticosterone (21-hydroxyprogren-4-ene-3,20-dione), cortisone (17,21-dihydroxyprogren-4-ene-3,11,20-trione), and cortisol (11β,17β,21-trihydroxyprogren-4-ene-3,20-dione). Trivial names for other steroids may be used provided that they are systematically defined in a single footnote. This footnote should also contain the definitions of all letter abbreviations. (In order to avoid ambiguity when both unsaturation and stereochemistry at a ring junction must be designated, the number of the carbon atom with the double bond should not be in the prefix, e.g., 5α-androst-16-en-3-one, not 16, 5α-androst-3-one.)

6. Trivial names may be modified by prefixes indicating substituents (as in 17β-hydroxyprogesterone for 17-hydroxyprogren-4-ene-3,20-dione), double bonds (as in 7-dehydrocholesterol for cholesta-5,7-dien-3β-ol) and epimeric configurations of functional groups provided the locus of epimerization is indicated (as in 3β-epiandrosterone for 3β-hydroxy-5α-androstan-17-one). Modified trivial names must never be more cumbersome than the systematic names they are intended to simplify. Such modified trivial names must be defined in terms of systematic names. Chemically impossible trivial names, e.g., 20-hydroxyprogesterone, are not acceptable.

7. When systematic names of steroid conjugates are defined, the rules recommended by IUPAC should be used. Those conjugates or mixtures of conjugates that are cleaved by β-glucuronidase are preferably referred to as glucosiduronates. However, since the correct structure of these conjugates is accurately known only infrequently, the other commonly used designations (e.g., glucuronide or glucuronoside) are also acceptable.

APPENDIX F

Nomenclature of Vitamin D Metabolites: Analogous and Structurally Related Compounds

vitamin D₃, cholecalciferol
vitamin D₂, ergocalciferol
25-hydroxyvitamin D₃, 25-hydroxycholecalciferol, 25OHD₃
25-hydroxyvitamin D₂, 25-hydroxyergocalciferol, 25OHD₂
25-hydroxyvitamin D₃, 25-hydroxycholecalciferol, 25OHD₃
1,25-dihydroxyvitamin D₃, 1,25-dihydroxycholecalciferol, 1,25-(OH)₂D₃
1,25-dihydroxyvitamin D₂, 1,25-dihydroxyergocalciferol, 1,25-(OH)₂D₂
1,25-dihydroxyvitamin D₃, 1,25-dihydroxycholecalciferol, 1,25-(OH)₂D₃
1,24,25-trihydroxyvitamin D₃, 1,24,25-trihydroxycholecalciferol, 1,24,25-(OH)₃D₃
24,25-dihydroxyvitamin D₂, 24,25-dihydroxycholecalciferol, 24,25-(OH)₂D₂
25,26-dihydroxyvitamin D₃, 25,26-dihydroxycholecalciferol, 25,26-(OH)₂D₃

APPENDIX G

Rapid Communications

Work submitted for consideration for publication as a Rapid Communication must be: 1) novel, 2) of exceptional significance, and 3) of interest to a broad segment of the endocrine community.

Justification for Rapid Communications. In a separate cover letter accompanying the Rapid Communication, the authors should justify the need for rapid publication of their findings and explain why publication as a comment, or as an original study, would be inappropriate. Rapid Communication manuscripts must be prepared using special forms available on request from the Editorial Office. Typing the manuscript on these forms is required for photo-offset reproduction. Manuscripts must not exceed three special form pages in length. The special pages will be reduced about 25 percent for publication. Instructions for preparation of Rapid Communication manuscripts will be included with the special forms. The original and three copies should be submitted. Manuscripts needing revision will be returned to the authors for retyping.
For your insulin-mixing or NPH-using patients

Humulin 70/30 makes life easier

Rapid onset and sustained duration insulin activity in a single vial

- May offer enhanced control through a more physiologic activity profile
- Accurate dosing—eliminates mixing errors
- Convenient premixed dose for better compliance
- Easy to use—for patients who find mixing difficult

Specify Humulin 70/30
70% human insulin isophane suspension
30% human insulin injection (recombinant DNA origin)

Humulin has just the right mix

Any change of insulin should be made cautiously and only under medical supervision.

Leadership In Diabetes Care

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Ethical Guidelines for Publications of Research

The Publications Committee has been keenly aware of the importance of formulating and disseminating rules of good conduct for authors, reviewers, and editors. Equally important is the establishment of due process for alleged or apparent improprieties. The Council of The Endocrine Society has approved the following Ethical Guidelines as prepared by the Publications Committee and has authorized periodic publication as well as distribution to members of our Editorial Boards, reviewers, and authors submitting manuscripts. The following statement is not meant to be all inclusive but is provided in sufficient detail to give a clear understanding of ethical considerations to all concerned.

The Publications Committee

Introduction

The Endocrine Society wishes to remind all of its members of the rules of good conduct as they apply to research and its publication. The fundamentals are honesty, fairness, good manners, and the subordination of self-interest to the common interest of our profession and of society. In these notes, the Publication Committee sets forth its rules of good conduct for authors, reviewers and editors.

I. Obligations of Authors

These things are forbidden:
1. submitting the work of others, in whole or in part, as one’s own. This is plagiarism (theft);
2. fabricating a report of research in whole or part. This is fraud (lying);
3. suppressing or altering data not in agreement with one’s hypothesis. This is dishonest and self-serving.

The author must show the editor written permission to quote any information learned personally from another investigator or by reviewing applications for research grants. In the introduction and especially in the discussion of a paper the author should cite fairly the work of others that is relevant either to the origin or to the outcome of the research described.

The author may invite as co-authors only those persons who have made significant intellectual and scientific contributions to the work reported. A co-author’s signature on the copyright release form submitted with the manuscript indicates that the co-author has had a part in the writing and final editing of the report, has been given a copy of the manuscript, and agrees to share responsibility and accountability for the results.

It is unethical to submit reports of the same or substantially overlapping research to more than one journal at the same time, unless the author can justify it in letters to both editors. Any preliminary accounts or abstracts of the work, already published, must be referenced in the complete report.

II. Obligations of Reviewers (Referees)

The critical review of manuscripts is an essential stage of publication. Every scientist has an obligation to do a fair share of reviewing.

The first obligation of a reviewer is to make expert, critical, and unbiased scientific and literary appraisals of reports of research in the fields of the reviewer’s knowledge and skills. The reviewer should return reviews promptly, within the editor’s deadline. If this cannot be done, the manuscript should be returned at once.

A reviewer should not attempt to review a manuscript if:
1. the reviewer does not feel competent to appraise the research described in it, or
2. reviewer feels there may be a conflict of interest or if the reviewer feels that a close personal or professional relationship with the author or co-author would bias judgment of the manuscript.

If there is any doubt about these prohibitions, the manuscript should be returned at once to the editor with an explanation. The editor should also be notified if the reviewer has previously reviewed the manuscript for another journal.

The reviewer’s criticisms of a manuscript, especially if the overall judgment is unfavorable, should be detailed and supported by appropriate references. The reviewer should note whether the work of others is properly cited. Any substantial resemblance of the manuscript being reviewed to a published paper or to a manuscript submitted at the same time to another journal must be reported to the editor.

Ordinarily, no part of the manuscript under review should be revealed to anyone. If a reviewer has a collaborator or consults a colleague on some special point, this fact, and the name of the collaborator or consultant, should be reported to the editor. With these exceptions, a reviewer must obtain through the editor the written permission of the authors to use or disclose any of the unpublished content of a manuscript under review.
III. Obligations of Editors

The editor directs and supervises the policies of a journal and is responsible for maintaining its scientific and literary quality.

The first obligation of an editor is to make certain that all authors receive confidential, expert, critical, and unbiased reviews of their work in a timely fashion.

The editor and members of the editor's staff should not disclose any information about a manuscript submitted for review to anyone except the reviewers or consultants.

An Editor may not take any part in the editorial management of any report of the editor's own research, since that involves conflict of interest. An editor must also avoid conflict of interest in the editorial management of reports of research closely related to the editor's own research. An editor may not use unpublished information of any kind from a submitted manuscript without written permission of the author.

If an editor is presented with convincing evidence that the main substance of conclusions of a report published in an editor's journal is erroneous, the editor should facilitate prompt publication of a report pointing out the error and, if possible, correcting it. The report may be written by the person who discovered the error or by an original author.

IV. Due Process

Reports of perceived improprieties or violation of the ethical guidelines presented above should be submitted with appropriate documentation either to the journal editor or to the Chairman of the Publications Committee. If the report goes first to the editor he will in turn submit it with appropriate additional information to the Publications Committee.

The Publications Committee, with advice and consent of the Council of The Endocrine Society, sets the policies and selects the editors of the journals and uses every fair means to maintain high standards of scientific reporting and literacy. The first obligation of the Committee to the public is to be truthful, consistent, and just. Therefore, alleged misconduct reported to the Committee will be investigated thoroughly.

The Committee investigation may include, but need not be limited to, correspondence and discussion with the individuals bringing the charge as well as those charged. If additional information needs to be developed from other sources, the Committee will do so, exercising discretion and recognizing that the investigation should cause minimal disruption and avoid harm to innocent parties.

When sufficient information is collected, the Committee will review the subject again, if necessary extending an invitation to the involved individual to appear before the Committee. The Committee will carefully assess the information available and attempt to establish the appropriateness and accuracy of the charge. If the misconduct appears to be confirmed, the Committee will refer the case to the Council with a recommended penalty.

Every effort should be made by the Committee to match the recommended penalty to the nature and seriousness of the misconduct. Penalties may, therefore, range from an official reprimand to dismissal from the Society. The penalty may also include temporary or permanent withdrawal of permission to publish in the journals of the Society. Consideration will also be given whether to recommend that a report of the findings and penalty be submitted to the Dean/Administrator/Chairman of the offender's institution.

The Council will review the report and recommendation of the Publications Committee and insure that all aspects of due process are fulfilled. If indicated, Council will appoint an ad hoc review committee. Council will protect the rights of the alleged offender by providing opportunity for appearance before the Council and the involvement in legal representation. The final decision and action on the charges will be made by Council.

Bibliography

In assembling these guidelines, the Publications Committee has made liberal use of the statement: "Ethical Guidelines to Publication of Chemical Research," prepared by the editors of the American Chemical Society and published in Accounts of Chemical Research, 1985, 18:355-357.

In addition, the Committee recommends reading the following:
1. Association of American Medical Colleges 1982 The maintenance of high ethical standards in the conduct of research.