A surprising fact is that testosterone is a more powerful stimulator of erythropoiesis in females than in males. \(^1\) \(^2\) We know several possible ways to account for this, but none of them proved or disproved. We know as well that it is not due to intrinsic differences in the erythropoietic marrow of the two sexes: male bone marrow can be transplanted into lethally irradiated females, where it is then as responsive to testosterone as is native female marrow. \(^2\)

Testosterone itself is a transient substance. Its biotransformation is so swift that it becomes virtually irrecoverable once tissue uptake has occurred. \(^3\) \(^4\) only its metabolites remain to show where it has been. Just possibly, some of these metabolites may be more important active agents than their short-lived precursor. All possible metabolites of testosterone can be formed in the liver. \(^4\) They are separable by paper chromatography into broad groupings that are either more polar or less polar than testosterone. \(^6\) \(^5\) and there is a sex difference in the groupings. \(^5\) The female liver tends to oxidize testosterone, producing 17-ketosteroids that are relatively nonpolar and non-\(^5\) \(^6\) and may be supposed to be strongly erythropoietic. Most of the metabolites produced by the male liver are polar \(^8\) and 17-hydroxylated. \(^5\) \(^6\) like the testosterone from which they descend, and some are androgenic. \(^4\)

Prepubertal males resemble females biochemically both in their erythropoietic response to androgens, and in the nonpolar way in which they handle testosterone. \(^5\) \(^7\) A major shift in this handling—a "tilt" towards polarity— is one of the important biochemical events of male puberty. \(^5\) \(^7\) If ketoconversion serves the young male and the female by negating the androgenicity of testosterone, this "tilt" now restores it, allowing expression of the virility which nature desires in the male.

Interestingly, pretreatment of female rats with phenobarbital for a time prior to testosterone administration has been shown to move the female metabolic pattern closer to the male polar pattern, while diminishing several of the effects of testosterone— including, perhaps, the erythropoietic effect. Phenobarbital is well known to be an active inducer of hydroxylating enzymes in the liver. \(^5\)

Possible Clinical Implications

Testosterone, because of its transient nature, is perhaps not the principle active substance we have long supposed it to be, but a precursor of other substances with important and distinctive activity profiles of their own. Some may embody just the erythropoietic effects of testosterone, or may at least eliminate much of its androgenicity. A difference between the male and female patterns of metabolizing testosterone, in conjunction with different male and female patterns of erythropoietic response to it, suggests that this may well be the case.

Deca-Durabolin is a potent erythropoietic agent with considerable reduction in androgenicity. In many patients with otherwise intractable anemias, Deca-Durabolin \(^10\) testosterone \(^11\) \(^12\) \(^14\) \(^19\) and other analogs \(^20\) \(^21\) have helped to reduce transfusion requirements and improve the hemoglobin, hematocrit and red-cell values—even in patients with the so-called "dialysis anemias" of chronic renal failure. Another important clinical advantage of Deca-Durabolin is that jaundice has not been associated with its use, even at the high dosage levels employed for certain refractory anemias.
CONTRAINDICATIONS:
1. Male patients with carcinoma of the prostate or breast.
2. Carcinoma of the breast in some females.
3. Pregnancy, because of masculinization of the fetus.
4. Nephrosis or the nephrotic phase of nephritis.

WARNING: Anabolic steroids do not enhance athletic ability.

PRECAUTIONS:
1. Hypercalcemia may develop both spontaneously and as a result of hormonal therapy in women with disseminated breast carcinoma. If it develops while on this agent, the drug should be stopped.
2. Caution is required in administering these agents to patients with cardiac, renal or hepatic disease. Edema may occur occasionally. Concomitant administration with adrenal steroids or ACTH may add to the edema.
3. If amenorrhea or menstrual irregularities develop the drug should be discontinued until the etiology is determined.
4. Anabolic steroids may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may have to be decreased in order to maintain the prothrombin time at the desired therapeutic level.
5. Anabolic steroids have been shown to alter glucose tolerance tests. Diabetics should be followed carefully and the insulin or oral hypoglycemic dosage adjusted accordingly.
6. Anabolic steroids should be used with caution in patients with benign prostatic hypertrophy.
7. Serum cholesterol may increase during therapy. Therefore, caution is required in administering these agents to patients with a history of myocardial infarction or coronary artery disease. Serial determinations of serum cholesterol should be made and therapy adjusted accordingly.

ADVERSE REACTIONS:
2. In Females: a. Hirsutism, male pattern baldness, deepening of the voice and clitoral enlargement. These changes are usually irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. b. Menstrual irregularities, c. Masculinization of the fetus.

SUPPLIED:
Deca-Durabolin (in sterile sesame oil solution for intramuscular injection) is available in a potency of 50 mg/cc with 10% benzyl alcohol (preservative):
1 cc: ampuls, box of 4.
2 cc: multiple dose vials.
Also available in a potency of 100 mg/cc with 10% benzyl alcohol (preservative):
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On a camping trip. Or at home. Koate® enables the hemophiliac to treat himself. Quickly. Safely. Conveniently.

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See sections entitled "Indications" and "Warning" for description of hepatitis risk.

THIS PRODUCT IS PREPARED FROM HUMAN VENOUS PLASMA. EACH INDIVIDUAL UNIT OF PLASMA HAS BEEN FOUND NONREACTIVE FOR HEPATITIS B SURFACE ANTIGEN USING THE RADIOIMMUNOASSAY METHOD. UNFORTUNATELY, THIS TEST DOES NOT PRECLUDE THE PRESENCE OF HEPATITIS VIRUS. SEE WARNING.

Indications
Antihemophilic Factor (Human). Koate® is indicated for the treatment of classical hemophilia (hemophilia A), in which there is a demonstrated deficiency of the plasma clotting factor. Factor VIII. Koate® provides a means of temporarily replacing the missing clotting factor in order to correct or prevent bleeding episodes or in order to perform emergency and elective surgery.

Warning
Koate® concentrate is a purified dried fraction of pooled plasma obtained from many paid donors. The presence of hepatitis virus should be assumed and the hazard of administering Koate® concentrate should be weighed against the medical consequence of withholding it, particularly in persons with few previous transfusions of blood and plasma products.

Kasper and Kipnis have concluded that those who had little exposure to blood products had a high risk of developing hepatitis after introduction of clotting factor concentrates, such as this product. For those patients, especially those with mild hemophilia, they recommend single donor products. However, for patients with moderate or severe hemophilia who have received numerous blood and plasma products, they feel that the risk of hepatitis is small. They believe that the clotting factor concentrates have greatly improved the management of severe hemophilia that these products should not be denied to appropriate patients.

Precautions
1. Antihemophilic Factor (Human). Koate® is intended for treatment of bleeding disorders arising from a deficiency in Factor VIII. This deficiency should be proven prior to administering Koate® since no benefit may be expected from its use in treating other causes of hemorrhage.
2. Antihemophilic Factor (Human). Koate® should be kept at a temperature below 2°C - 8°C (35°F - 46°F) until reconstituted for use. After reconstitution, administer promptly (within 3 hours). Do not refrigerate after reconstitution. NOTE: The recommendation to administer promptly after reconstitution is intended to avoid the ill effect of any possible bacterial contamination occurring during reconstitution. Koate® is fully stable, without potency loss for at least 24 hours at room temperature after reconstitution.
3. Administer only by the intravenous route.
4. A filter should be used prior to administering the reconstituted Koate® solution. This may be accomplished by using the enclosed sterile filter needle. See Reconstitution and Administration directions.
5. Koate® contains measurable levels of blood group antigens which are not clinically significant when controlling relatively minor bleeding episodes. When large or frequently repeated doses are required in patients of blood groups A, B, or AB, the possibility of intravascular hemolysis should be considered.
6. Administration equipment and any reconstituted Koate® not used should be discarded.

Adverse Reactions
No severe adverse reactions were reported during the clinical trials of Koate®. One patient experienced transient chest discomfort and cough beginning 20 minutes after infusion and lasting for one hour. During subsequent infusions this patient had no further reactions. A second patient developed transient dizziness following each of eight infusions. Mild allergic reactions may result from the administration of AHF preparations.

When large or frequently repeated doses are required in patients other than those of blood type O, there is a possibility of intravascular hemolysis. Should this condition occur leading to progressive anemia, administration of serologically compatible type O packed red blood cells should be considered. Also the administration of type-specific cryoprecipitate has been recommended for maintaining adequate Factor VIII levels.

How Supplied
Antihemophilic Factor (Human). Koate® is supplied in single dose bottles with the total units of Factor VIII activity and total grams of protein stated on the label of each bottle. A suitable volume of Sterile Water for Injection, U.S.P., and a sterile filter needle is provided.

Limited Warranty
A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration, and biologic differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use, and that the risk of transmitting hepatitis be carefully weighed before the product is prescribed.

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BLOOD GASES IN CLINICAL PRACTICE by Leopoldo Lapuerta, Univ. of Texas Medical School, San Antonio. Foreword by Sydney Schiffer. The subject of blood gases is discussed in this volume in an eminently practical manner. The approach is simple and basic; the style clear and straightforward. The initial chapter reviews the necessary physical and chemical concepts. This is followed by data on the interpretation of blood gases, symptoms caused by their abnormalities, and rational therapeutic approaches to derangements of ventilation, oxygenation and acid-base balance. The remainder of the text, more than half the book, reviews in detail the practical use of blood gases in a variety of clinical situations. These range from the classic subjects of respiratory failure and pulmonary edema to conditions in which the usefulness of blood gases is less well known but still very important, such as epileptic convulsions and kyphoscoliosis. ’76, 132 pp., 9 il., 8 tables, $12.50

CLOT by James L. Tullis, New England Deaconess Hospital, Boston, Massachusetts. Chapters by Francis C. Chao. This is a valuable reference for all those concerned with clotting and hemostasis. Emphases include the molecular characterization of clotting factors and applied aspects of the management of patients with bleeding and clotting disorders. The clinical discussion includes the principal bleeding states associated with clotting deficiencies and the management of hypercoagulability and thrombosis. ’76, 592 pp., 17 il. (4 in color), 23 tables, $39.50

WAVEFORM ANALYSIS IN MEDICINE: An Introduction by R. David Petersen, Atlanta, Georgia, and Joseph C. Myers, Univ. of Nebraska, Lincoln. This how-to-do-it approach to waveform analysis in medicine helps to bridge the vocabulary gap between the engineer and the physician. Mathematical proofs are supplanted by easily understood diagrams. Topics of discussion include instrumentation and power spectral density of waveforms, the use of the analog computer in deriving mathematical equations for given waveshapes, and the use of calculus in waveform analysis. Although designed primarily for health professionals, this book will also be useful to undergraduates and graduates in engineering. ’76, 308 pp., 121 il., 10 tables, $24.75
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Desferal has been shown to be an effective therapeutic agent for chelating damaging iron stores and allowing their excretion from the body. Desferal can help reduce the massive burden of iron overload in thalassemia.

CIBA hopes the availability of Desferal can play a role in reducing the grave consequences of this damaging disease. If Desferal is relevant to your practice, write us. Detailed information on it is now available.
Desferal® mesylate (deferoxamine mesylate USP)

DESCRIPTION
Desferal is available as the mesylate salt of deferoxamine. Its solubility in water is greater than 25%; 500 mg will dissolve in 2 ml distilled water.

Chemically it is N-[5-[15-Aminopentyl]- hydroxy carbamoyl]- propionamido] pentaetyl]-3-[5-(N-hydroxyacetamido) pentaetyl]- carbamoyl]propionyloxyhydroxamic acid monomethanesulfonate (salt).

ACTIONS
Desferal is a compound with a specific ability to chelate iron, forming a stable complex which prevents its iron from entering into further chemical reactions. This chelate is readily soluble in water and passes easily through the kidney, giving the urine a characteristic reddish color. Some is also excreted in the feces via the bile. Theoretically, 100 parts by weight of Desferal are capable of binding approximately 8.5 parts by weight of ferric iron. In studies thus far in man and animals, Desferal does not cause any demonstrable increase in the excretion of electrolytes and trace metals.

INDICATIONS
To facilitate the removal of iron in the treatment of acute iron intoxication and in chronic iron overload due to transfusion-dependent anemias.

ACUTE IRON INTOXICATION
Desferal is an adjunct to, and not a substitute for, standard measures generally used in treating acute iron intoxication which may include the following:
1. Induction of emesis with syrup of ipecac.
2. Gastric lavage.
3. Suction and maintenance of clear airway.
4. Control of shock with intravenous fluids, blood, oxygen, and vasopressors.
5. Correction of acidosis.

CHRONIC IRON OVERLOAD
Desferal can promote iron excretion in patients who have secondary iron overload from multiple transfusions (such as occur in the treatment of thalassemia and other chronic anemias). One controlled study has found that long-term therapy with Desferal slows accumulation of hepatic iron and retards or eliminates progression of hepatic fibrosis. Desferal is not indicated for the treatment of primary hemochromatosis, since phlebotomy is the method of choice for removing excess iron in this indication.

CONTRAINDICATIONS
Desferal is contraindicated in patients with severe renal disease or anuria, since the drug and the chelate which it forms with iron are excreted primarily by the kidney.

WARNING
Rarely, cataracts have been observed in patients who received the drug over prolonged periods in the treatment of chronic iron storage diseases. Stiff lamp examinations performed in patients treated with Desferal for acute iron intoxication have not revealed cataracts.

Usage in Pregnancy
Skeletal anomalies were noted in the fetuses of two animal species at doses just above those recommended for humans. Therefore, Desferal should not be administered to women of childbearing potential, particularly during early pregnancy, except when in the judgment of the physician the potential benefits outweigh the possible hazards.

PRECAUTIONS
Flushing of the skin, urticaria, hypotension, and even shock have occurred in a few patients when Desferal has been administered by rapid intravenous injection. To avoid these reactions, Desferal should be given intramuscularly or by slow intravenous infusion.

ADVERSE REACTIONS
Occasionally, pain and induration at the site of injection have been reported. Side effects reported in patients treated for acute iron intoxication include generalized erythema, urticaria, and hypotension, which occurred with rapid intravenous injection. Adverse effects reported in patients receiving long-term therapy for chronic iron storage diseases include allergic-type reactions (cutaneous wheal formation, generalized itching, rash, anaphylactic reaction), blurring of vision, dysuria, abdominal discomfort, diarrhea, leg cramps, tachycardia, and fever. These reactions might also occur in an occasional patient treated for acute iron intoxication.

DOSE AND ADMINISTRATION
Since little of the drug is absorbed when administered orally, it is necessary to administer Desferal parenterally to chelate the iron that has been absorbed.

ACUTE IRON INTOXICATION

Intramuscular Administration
Intramuscular administration is preferred and should be used for all patients not in shock.

Dose: One Gm should be administered initially. This may be followed by 0.5 Gm every four hours for two doses, depending upon the clinical response, subsequent doses of 0.5 Gm may be administered every four to twelve hours. The total amount administered should not exceed 6 Gm in twenty-four hours.

Preparation of Solution for Intramuscular Administration: Dissolve the Desferal by adding 2 ml sterile water for injection to each ampul. Make sure that solution is complete and then withdraw the drug and administer intramuscularly.

Intravenous Administration
This route should be used only for patients in a state of cardiovascular collapse and then only by slow infusion. The rate of infusion should not exceed 15 mg/kg/hour.

Dose: An initial dose of 1 Gm should be administered at a rate not to exceed 15 mg/kg/hour. This may be followed by 0.5 Gm every four hours for two doses. Depending upon the clinical response, subsequent doses of 0.5 Gm may be administered every four to twelve hours. The total amount administered should not exceed 6 Gm in twenty-four hours. As soon as the clinical condition of the patient permits, intravenous administration should be discontinued and the drug administered intramuscularly.

Preparation of Solution for Intravenous Administration: Dissolve the Desferal by adding 2 ml sterile water for injection to each ampul. Make sure that solution is complete and then withdraw the drug and add to physiologic saline, glucose in water, or Ringer's lactate solution and administer at a rate not to exceed 15 mg/kg/hour.

CHRONIC IRON OVERLOAD
Doses: 0.5 to 0.1 Gm daily administered intramuscularly. In addition, 2.0 Gm should be administered intravenously with, but separate from, each unit of blood transfused. The rate of intravenous infusion must not exceed 15 mg/kg/hour.

Note: Desferal reconstituted with sterile water may be stored under sterile conditions and protected from light at room temperature for not longer than one week.

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International Histological Classification of Tumours No. 14

HISTOLOGICAL AND CYTOLOGICAL TYPING OF NEOPLASTIC DISEASES OF HAEMATOPOIETIC AND LYMPHOID TISSUES

by G. MATHÉ & H. RAPPAPORT
in collaboration with
G. T. O'CONOR & H. TORLONI
and haematologists and pathologists in 5 countries

This volume in the WHO series, INTERNATIONAL HISTOLOGICAL CLASSIFICATION OF TUMOURS, is the outcome of 12 years' work by the WHO Centre for the Histological and Cytological Classification of Neoplastic Diseases of Haematopoietic and Lymphoid Tissues, established at the Institut de Cancérologie et d'Immunogénétique, Groupe hospitalier Paul-Brousse, Villejuif, France.

The classification is based primarily on the predominating component cell type, but the main clinical and gross morphological patterns are also taken into account, initially localized tumours being grouped separately from diseases apparently systemic from onset. The roles of histopathology and cytology in diagnosis are both emphasized and illustrated. Information on T and B cell immunological markers is also presented.

Classification of haematopoietic and lymphoid neoplastic diseases is currently in an unstable state owing to fast moving developments in this field. New histogenetic and immunological concepts are being formulated at a rapid rate. Even during the course of the preparation of this publication, a number of new nosological approaches have been put forward. The results of several international workshops and meetings have therefore played a role in the formulation of the classification. Although there is still lack of agreement in several areas, particularly for the non-Hodgkin's lymphomas, it is felt that publication at this stage would have the benefit of providing a degree of stability in the recording of comparable data while conceptual work continues in this field.

The book is illustrated with 124 colour photomicrographs, which are also available in the form of 35-mm transparencies for teaching purposes.

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Proceedings of the Third Irwin Strasburger Memorial Seminar on Immunology

Edited by
STEPHEN D. LITWIN, M.D., CHARLES L. CHRISTIAN, M.D. AND GREGORY W. SISKIND, M.D.

Based on a symposium held at Cornell University Medical College during 1976, this volume attempts to examine critical issues and highlights of the field rather than to survey all present knowledge. The chapters deal with a series of recent advances in clinical immunology. In particular, the identification, characterization and isolation of different subpopulations of human lymphocytes is discussed in considerable detail. The genetic control and biological significance of the major histocompatibility system in man is examined in the light of current immunological theory. Specific methods for the clinical evaluation of immune function in man, including skin testing, evaluation of serum immunoglobulin levels and the responses of human lymphocytes to mitogens is given intensive coverage. Finally, a review of the cellular basis of human immune activity is presented.

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Factor VIII or IX

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<td>25.00</td>
<td>250 ml – 225.00</td>
</tr>
<tr>
<td>25 ml</td>
<td>45.00</td>
<td>500 ml – 400.00</td>
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<tr>
<td>50 ml</td>
<td>75.00</td>
<td>1000 ml – 750.00</td>
</tr>
<tr>
<td>100 ml</td>
<td>125.00</td>
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</tbody>
</table>

- All shipments are packed with dry ice in styrofoam boxes. (Handling Charge $10.00 for orders under $150.00). Shipments within the United States are delivered within 24 hours.
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The second page should contain an abstract of 200 words or less, summarizing the reason for the study, the methods used, the results, and the major conclusions. Do not include a summary at the end of the paper. The remainder of the paper should be written as concisely as possible.

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Journal article, two or more authors:


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Chapter of book:


Chapter of book that is part of published meeting:


(Continued on page xxiv)
When you suspect sickle cell or other hematologic disorders . . .
turn to Saunders—for answers!

BUNN, FORGET & RANNEY:
Hemoglobinopathies—Major Problems in Internal Medicine, 12

The pathogenesis and treatment of sickle cell anemia and other hemoglobinopathies are examined in this decidedly clinical book. The authors first discuss the structure, function and biosynthesis of normal hemoglobin; then they describe other human hemoglobin variants. Sickling disorders, unstable hemoglobins, the methemoglobinemias, and variants with abnormal oxygen binding are treated. This volume is an abridgment of Bunn, Forget & Ranney’s Human Hemoglobinins, which features more complete coverage of the structure, function and synthesis of hemoglobins.

By H. Franklin Bunn, MD, Assoc. Prof. of Medicine, Harvard Medical School; Bernard G. Forget, MD, Assoc. Prof. of Medicine, Yale Medical School; and Helen M. Ranney, MD, Prof. and Chairman, Dept. of Medicine, Univ. of California, San Diego. 308 pp. Illustd. $18.00. March 1977. Order #2179-1.

BUNN, FORGET & RANNEY: Human Hemoglobins

This volume presents an in-depth, detailed look at the human hemoglobins. The first four chapters present basic information on normal human hemoglobin including structure, function, physiology, biosynthesis and genetics. Then the following five chapters introduce various clinical disorders: thalassemias, sickle cell anemias and other hemoglobinopathies.

By H. Franklin Bunn, MD; Bernard G. Forget, MD; and Helen M. Ranney, MD. About 415 pp. Illustd. About $20.00. Just Ready. Order #2178-3.

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Edited by M. C. G. Israels, MD, FRCP, Emeritus Prof. of Clinical Haematology; and I. W. Delamore, PhD, FRCP, FRCPath, Physician in Charge, Univ. Dept. of Clinical Haematology, The Royal Infirmary, Manchester; Lecturer in Clinical Haematology, both of the Univ. of Manchester; with 22 other contributors. 545 pp. Illustd. $27.50. Dec. 1976. Order #5047-3.

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Chapter of book that is part of unpublished meeting:


ABSTRACTS AND LETTERS TO EDITORS:


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RECOMMENDATION FOR USAGE OF UNITS

The International Committee for Standardization in Hematology has recommended that the following units be used in the hematologic literature.

<table>
<thead>
<tr>
<th>Component</th>
<th>Normal Range in SI Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>14.4 g/dl(^*),(^+)</td>
</tr>
<tr>
<td>RBC (RCC)</td>
<td>(4.5 \times 10^{12}/l)</td>
</tr>
<tr>
<td>PCV</td>
<td>0.41 (^*),(^+)</td>
</tr>
<tr>
<td>MCV</td>
<td>75-95 g/l§</td>
</tr>
<tr>
<td>MCH</td>
<td>27-32 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>30-35 g/dl</td>
</tr>
<tr>
<td>WBC (WCC)</td>
<td>4.0-11.0 (\times 10^{9}/l)</td>
</tr>
<tr>
<td>Platelets</td>
<td>150-400 (\times 10^{9}/l)</td>
</tr>
<tr>
<td>Red cell diameter</td>
<td>6.7-7.7 (\mu m)</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>0.2-2.0%(^*)</td>
</tr>
<tr>
<td></td>
<td>10-100 (\times 10^{9}/l)</td>
</tr>
<tr>
<td>Serum iron</td>
<td>14-29 (\mu mol/l)(\times)</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>45-72 (\mu mol/l)(\times)</td>
</tr>
<tr>
<td>Transferrin</td>
<td>1.2-2.0 g/l</td>
</tr>
<tr>
<td>Serum haptoglobins (Hb binding)</td>
<td>0.3-2.0 g/l</td>
</tr>
<tr>
<td>Serum (B_{12}) (as cyanocobalamin equivalents)</td>
<td>160-925 ng/l</td>
</tr>
<tr>
<td>Serum folate</td>
<td>3-20 (\mu g/l)</td>
</tr>
<tr>
<td>Plasma fibrinogen</td>
<td>1.5-4.0 g/l</td>
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* As the normal range varies with age and sex, only one measurement in the normal range has been given as an example.
\(^+\) dl, deciliter.
\(^\times\) (3) No unit necessary; l/l is implied.
\(§\) fl = femtoliter.
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