Imferon®
(Iron dextran injection USP)

WARNING:

THE PARENTERAL USE OF COMPLEXES OF IRON AND CARBOHYDRATES HAS RESULTED IN FATAL ANAPHYLAC-
TIC-TYPE REACTIONS. DEATHS ASSOCIATED WITH SUCH
ADMINISTRATION HAVE BEEN REPORTED THEREFORE.
IMFERON SHOULD BE USED ONLY IN THOSE PATIENTS
WHERE CLEARLY ESTABLISHED INDICATIONS EXIST. CONFIR-
MED BY APPROPRIATE LABORATORY INVESTIGATIONS
CORROBORATING IRON DEFICIENCY ANEMIA NOT AMENA-
BLE TO ORAL IRON THERAPY.

ACTION: The iron dextran complex is dissociated by the reticuloen-
dotheial system, and the ferric iron is transported by transferrin and
incorporated into hemoglobin.

INDICATIONS: For the treatment of iron deficiency anemia: intra-
muscular or intravenous injections of iron are advisable solely for
use in those patients in whom iron deficiency anemia is present, its
discrete cause has been determined and, if possible, corrected, and in whom
oral administration of iron is unsatisfactory or impossible, for
example: intolerance to oral preparation, resistance to oral
iron therapy, rapid replacement of iron stores in selected patients in whom
oral therapy is ineffective, such as hypochromic anemia of
infancy and hypochromic anemia of the last trimester of pregnancy;
selected hemorrhagic cases (appropriate steps should be taken to
correct and prevent any excessive blood loss that may have been
reversed as an etiologic factor), to replace post-operative transfu-
sion to some degree, in those patients who cannot be relied upon
to take oral medication.

IMFERON (iron dextran injection) injected intramuscularly is the
preferred and recommended route of administration. Intravenous
use of IMFERON should be limited to the following circumstances:
A. Deficient in muscle mass for deep intramuscular injection
B. Impaired absorption from the muscle due to scars or edema
C. Possibility of uncontrolled intramuscular bleeding due to
trauma as may occur in hemophilia
D. Where massive and prolonged parenteral therapy is indicated as
may be necessary in instances of chronic subclinical blood loss,
such as familial telangiectasia.
E. In those circumstances where, in the opinion of the physician, the
benefit of intravenous administration substantially outweighs the
risk.

CONTRAINDICATIONS: Hypersensitivity to the product. All anemias
other than iron deficiency anemia.

WARNINGS: This preparation should be used with extreme care in the
presence of serious impairment of liver function.

A Risk of carcinogenesis may attend the intramuscular injection of
iron-carbohydrate complexes. Such complexes have been found
under experimental conditions to produce sarcomas when injected
in rats, mice and rabbits, and possibly in hamsters, in very large
doses. The number of tumors produced was relatively small, and
such tumors have not been produced in guinea pigs. The long latent
period between the injection of a potential carcinogen and the
appearance of a tumor makes it impossible as yet to measure the risk
in man. However, the risk of carcinogenesis in man, following
recommended therapy, appears to be extremely small.

Usage in Pregnancy: In animals, fetal abnormalities have been
demonstrated when IMFERON (iron dextran injection) was given early
in pregnancy. Safe use of IMFERON has not been established with
respect to adverse effects on human fetal development. IMFERON
should not be used in early pregnancy and should be used in women of
child-bearing potential only when, in the judgment of the physi-
cian, the potential benefits outweigh the possible hazards.

PRECAUTIONS: Unwarranted therapy with parenteral iron will cause
excess storage of iron with the consequent possibility of exogenous
hemodilution. Such iron overload is particularly apt to occur in
patients with hemoglobinopathies and other refractory anemias
which might be erroneously diagnosed as iron deficiency anemias.

Patients with iron deficiency anemia and rheumatoid arthritis may
have an acute exacerbation of joint pain and swelling following the
intravenous administration of IMFERON (iron dextran injection).

ADVERSE REACTIONS: Anaphylactic reactions including fatal ana-
phylaxis, severe febrile reactions, arthralgia and myalgia, variable
degree of soreness and inflammation at injection site (IM injection),
brown skin discoloration at injection site (IM injection), local
phlebitis at injection site (IV injection), peripheral vascular "flush-
ing" with rapidly rapid IV administration, hypotension, and
possible arthritic reactivation in patients with quiescent rheumatoid
arthritis, minor reactions may include headache, transitory pares-
thesia, nausea, shivering, itching, and rash.

DOSAGE AND ADMINISTRATION: Periodic hematologic determina-
tions are to be used as a guide in therapy, bearing in mind that iron
storage may lag behind the appearance of normal blood morphology.
Since each course of iron must be individualized, refer to the
package insert for complete directions for intramuscular and intra-
venous use.

5-8989 (7985)

ACADEMIC PRESS
A Subsidiary of Harcourt Brace Jovanovich, Publishers
111 Fifth Avenue, New York, N. Y. 10003
24-28 Oval Road, London NW1 7DX

BLOOD—THE JOURNAL OF THE ASH

Edited by DOUGLAS MacN. SURGENOR
Department of Biochemistry
School of Medicine
State University of New York at Buffalo
Buffalo, New York

FROM A REVIEW OF THE FIRST EDITION:
‘The Editor’s aim in launching this major work was to
present a single volume as complete a picture as of
many aspects as possible of the biology of the red blood
The result...is packed with information
and splendidly illustrated and produced.’—BRITISH JOURNAL OF HAEMATOLOGY

The Second Edition of THE RED BLOOD CELL has
been completely revised and greatly enlarged in
order to provide the latest information on all aspects
of red cell biology—composition, metabolism, func-
tion, immunological and suspension behavior.

THE RED BLOOD CELL is essential reading for
basic and clinical investigators using the red cell as
an experimental model. It is aimed at the investigator
who needs comprehensive, in-depth knowledge
about particular aspects of the erythrocyte, and will
be of great interest to hematologists, pathologists,
biochemists, physiologists, biophysicists, and
biologists.

VOLUME 2/ 1975, 725 pp., $49.50/213.75
Subscription price $42.00/120.20*

*Subscription prices for individual volumes valid only on orders for
the complete set received before publication of the last volume.

Prices subject to change without notice.

APPLEACEM PRESS

Merrell NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215
For Iron Deficiency Anemia Not Amenable To Oral Therapy*

**Imferon IM/IV (Iron dextran injection)**

each ml contains 80 mg elemental iron as an iron dextran complex

Iron By Injection For

Indications and Directions for Use

This One

NKR9-85C-SJ83
BLOOD
The Journal of
The American Society of Hematology

Blood: The Journal of The American Society of Hematology is published monthly, in two volumes per year.

Editorial correspondence should be addressed to Dr. Ernst R. Jaffé, Albert Einstein College of Medicine of Yeshiva University, 1300 Morris Park Avenue, Bronx, N.Y. 10461, telephone (212) 430-4040.

Business correspondence should be addressed to Grune & Stratton, Inc., Medical Publishers, 111 Fifth Avenue, New York, N.Y. 10003.

Subscription rates: $45.00 per year within the United States; foreign, $48.50 per year. Students, Research Fellows, Interns, and Residents may receive a reduced subscription rate: $35.00 per year within the United States; foreign, $38.50 per year. A letter giving qualifying data must accompany such orders. Single copies: $6.00; foreign, $6.50. Subscriptions are accepted on a calendar-year basis. Prices are subject to change. Back-issue and back-volume prices are those in current effect.

Advertising Representative: Charles C. Cunningham, Inc., P.O. Box 308, Park Ridge, New Jersey 07656, telephone (201) 391-3210.

Change-of-address notices, including both the subscriber's old and new address, should be sent to the publisher at least one month in advance.


Postmaster: Send 3579 to 300 West Chestnut St., Ephrata, Pa. 17522. Return postage guaranteed.

Second-class postage paid at New York, N.Y., and at additional mailing offices.
active against a number of solid tumors as well as certain hematologic malignancies

In addition to osteogenic sarcoma, neoplastic conditions that have responded to Adriamycin include: acute lymphoblastic leukemia, acute myeloblastic leukemia, Wilms' tumor, soft tissue sarcoma, neuroblastoma, ovarian carcinoma, transitional cell bladder tumor, bronchogenic lung carcinoma, thyroid carcinoma, lymphoma of both Hodgkin and non-Hodgkin type and breast carcinoma.

Like other cytotoxic agents, Adriamycin should be used only under the direction of specialists qualified in the administration of such drugs.

Severe local tissue necrosis will occur if there is extravasation during administration.

Serious irreversible myocardial toxicity has occurred, especially in patients who have received more than the recommended cumulative dosage.

The incidence of bone marrow depression is high. Hematopoietic toxicity may limit dosage.

In patients with impaired hepatic function, dosage should be reduced.

Complete alopecia usually accompanies treatment. Stomatitis and esophagitis are common.

For information on the use of Adriamycin, call collect (302) 575-7830.

Or, fill out and mail the coupon below.

For complete prescribing information, please see the following page.
ADRIAMYCIN™ (doxorubicin hydrochloride) for injection
FOR INTRAVENOUS USE ONLY

WARNINGS
1. Severe local tissue necrosis will occur if there is extravasation during administration. Adriamycin must not be given by the intradermal or subcutaneous route.
2. Serious irreversible myocardial toxicity with delayed congestive failure often unresponsive to any cardiac supportive therapy may be encountered as total dosage approaches 550 mg/m². This toxicity may occur at lower cumulative doses in patients with prior mediastinal irradiation or on concurrent cyclophosphamide therapy.
3. Doxorubicin should be reduced in patients with impaired hepatic function.
4. Severe myelosuppression may occur.
5. Adriamycin should be administered only under the supervision of a physician who is experienced in the use of cancer chemotherapy agents.

DESCRIPTION
Doxorubicin hydrochloride is isolated from cultures of Streptomyces peucetius var caesius. It is supplied in the hydrochloride form as a freeze-dried powder containing lactose. Doxorubicin hydrochloride is readily soluble in water or physiological saline.

CLINICAL PHARMACOLOGY
Though not completely elucidated, the mechanism of action of doxorubicin is related to its ability to bind to DNA and inhibit nucleic acid synthesis. Cell culture studies have demonstrated rapid cell penetration and perinuclear chromatin bridging, rapid inhibition of mitotic activity and nucleic acid synthesis, mutagenesis, and chromosomal aberrations. Adriamycin has shown a significant effect in a variety of experimental tumors, immunsuppressive, carcinogenic properties in rodents, induction of a variety of toxic effects, including cardiac toxicity in rabbits, myelosuppression in all species and anaphylactic reactions in rats and dogs. Teratology studies, though not showing a definite increase in specific or non-specific malformations, indicate a moderate interference with the viability of embryos and fetuses.

Pharmacokinetic studies show the intravenous administration of normal or radioisotoped Adriamycin (doxorubicin hydrochloride) for injection is followed by rapid plasma clearance and significant tissue binding. Urinary excretion, as determined by fluorimetric methods, accounts for approximately 4-5% of the administered dose in 24 hours. Adriamycin represents the major excretion route. 40-50% of the administered dose being recovered in the bile or the feces in seven days. Immunosuppression of liver function results in slower excretion, and consequently, increased retention and accumulation in plasma and tissue. Adriamycin does not cross the blood-brain barrier.

INDICATIONS
Adriamycin has been used successfully to produce regression in neoplastic conditions such as acute lymphocytic leukemia, acute myelocytic leukemia, Wilms tumor, urinary neoplasms, soft tissue and bone sarcomas, breast carcinoma, ovarian carcinoma, transitional cell bladder carcinoma, bronchogenic lung carcinoma, thyroid carcinoma and lymphomas of both Hodgkin and non-Hodgkin types. A number of other solid tumors have also shown some responsiveness but in numbers not limited to justify specific recommendations. Studies to date have shown malignant melanoma, kidney carcinoma, large bowel carcinoma, brain tumors and metastases to the central nervous system not to be significantly responsive to Adriamycin therapy.

CONTRAINDICATIONS
Adriamycin therapy should not be started in patients who have marked myelosuppression induced by previous treatment with other antineoplastic agents or by radiotherapy. Conclusive data are not available on pre-existing heart disease as a co-factor of increased risk of Adriamycin-induced cardiac toxicity. Preliminary data suggest that in such cases cardiac toxicity may occur at doses lower than the recommended cumulative limit. It is therefore not recommended to start Adriamycin in such cases. Adriamycin treatment is contraindicated in patients who received previous treatment with complete cumulative doses of Adriamycin and daunorubicin.

WARNINGS
Special attention must be given to the cardiac toxicity exhibited by Adriamycin. Although uncommon, acute or ventricular failure has occurred, particularly in patients who have received total dosage of the drug exceeding the currently recommended limit of 550 mg/m² of body surface. This limit appears to be lower in children who received radiotherapy to the mediastinal area. The total dose of Adriamycin administered to the individual patient should also take into account any previous or concurrent therapy with other potentially cardiotoxic agents such as cyclophosphamide or related compounds such as daunorubicin. It should be noted that the cardiac failure may also occur several weeks after administration of the drug and is often not favorably affected by presently known medical or physical therapy for cardiac support. Early clinical diagnosis of drug-induced heart failure appears to be essential for successful treatment with digitalis, diuretics, low salt diet and bed rest. Severe cardiac toxicity may occur precipitously without antecedent EKG changes. Baseline EKG and periodic follow-up EKG during, and immediately after, active drug therapy is an advisable precaution. Transient EKG changes, such as T wave flattening, S-T depression, and arrhythmias are presently not considered indicators for suspension of Adriamycin therapy. A reduction in the voltage of the QRS wave is presently considered more specifically predictive for cardiac toxicity if this occurs, the benefit of continued therapy must be carefully evaluated against the risk of producing reversible cardiac damage.

There is a high incidence of bone marrow depression, primarily of leukocytes, requiring careful hematopoietic support. With the recommended dosage schedule, leukopenia is usually transient, reaching its nadir at 10-14 days after treatment with recovery usually occurring by the 21st day. White blood cell counts as low as 1000/mm³ are to be expected during treatment with appropriate doses of Adriamycin. Hematologic and platelet levels should also be monitored since they may also be depressed. Hematotoxicity may require dose reduction or suspension or delay of Adriamycin therapy. Persistent severe myelosuppression may result in superinfection or hemorrhage.

Toxicity recommended doses of Adriamycin is enhanced by hepatic impairment. Therefore, prior to the individual dosing, evaluation of hepatic function is recommended using conventional clinical laboratory tests such as SGPT, SGOT, alkaline phosphatase, bilirubin, and BSP (see DOSAGE AND ADMINISTRATION).

On intravenous administration of Adriamycin, a stinging or burning sensation signifies a small degree of extravasation and even blood return from aspiration of the infusion needle is good. The injection or infusion should be immediately terminated and restarted in another vein.

PRECAUTIONS
Initial treatment with Adriamycin requires close observation of the patient and extensive laboratory monitoring. It is recommended, therefore, that patients be hospitalized at least during the first phase of the treatment.

There is no adequate information on whether this drug may adversely affect fertility in human males or females, or have a teratogenic potential or other adverse effects on the fetus. Experimental data, however, suggest that Adriamycin may reduce the viability of the tissues, therefore the benefits to the pregnant patient should be weighed against the potential toxicity to fetus and embryo. Adriamycin and related compounds have also been shown to have mutagenic and carcinogenic properties when tested in experimental models.

Adriamycin imparts a red coloration to the urine for 1-2 days after administration and patients should be advised to expect this during active therapy.

Adriamycin is not an antimicrobial agent.

ADVERSE REACTIONS
Dose-limiting toxicities of therapy are myelosuppression and cardiotoxicity (see WARNINGS). Other reactions reported are:

Cardiovascular—Reversible complete atrioventricular block occurs in most cases. Hypoperfusion of skin and mucous membranes, primarily in children in a few cases. Recall of skin reaction due to prior radiod decadation has occurred with Adriamycin administration.

Gastrointestinal—Acute nausea and vomiting occurs frequently and may be severe. This may be alleviated by antiemetic therapy. Myocarditis (stomatitis and esophagitis) may occur 5-10 days after administration. The effect may be severe leading to dilatation and rupture of a major vessel or S-P infections. The incidence and severity of myelosuppression is greater with the 3 successive daily dosage regimen. Anorexia and diarrhea have been occasionally reported.

Vascular—Phlebitis/thrombosis has been reported especially when small veins are used as a single vein is used for repeated administration. Facial flushing may occur if the injection is given too rapidly.

Hypersensitivity—Fever, chills and artricular have been reported occasionally. Anaphylaxis may occur.

Other—Conjugates and lactation occur rarely.

DOSAGE AND ADMINISTRATION

Preparation of Solution: Adriamycin should be reconstituted with Sodium Chloride Injection U.S.P. as indicated in the Dilation Table.

Dilation Table

<table>
<thead>
<tr>
<th>Dilation Size</th>
<th>Concentration</th>
<th>Volume to Be Added</th>
<th>Vial Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 ml</td>
<td>2 mg/ml</td>
<td>5 ml</td>
<td>10 mg</td>
</tr>
<tr>
<td>10 ml</td>
<td>2 mg/ml</td>
<td>10 ml</td>
<td>20 mg</td>
</tr>
<tr>
<td>20 ml</td>
<td>2 mg/ml</td>
<td>20 ml</td>
<td>50 mg</td>
</tr>
</tbody>
</table>

If Adriamycin powder or solution contacts the skin or mucous, wash thoroughly with soap and water. After adding the diluent, the vial should be shaken and the contents allowed to dissolve. The reconstituted solution is stable for 2 hours at room temperature and 24 hours under refrigeration (2-8°C). It should be protected from exposure to sunlight and any unused solution should be discarded.

It is recommended that Adriamycin be administered into the tubing of a freely running intravenous infusion of Sodium Chloride Injection U.S.P. or the percent (5%) Dextrose Injection U.S.P. This procedure will reduce likelihood of extravasation and consequent tissue damage.

Adriamycin should not be mixed with heparin since it has been reported that these drugs are incompatible to the extent that a precipitate may form. Until specific compatibility data is available, it is not recommended that Adriamycin be mixed with other drugs.

Adriamycin has been used in combination with other approved chemotherapeutic agents. Though evidence is available that at least in some types of neoplastic disease combination chemotherapy is superior to single agents, the benefits and risks of such therapy have not yet been fully elucidated.

HOW SUPPLIED

ADRIAMYCIN™ (doxorubicin hydrochloride) for injection is available in two sizes.

10 mg—Each rubber disc-capped vial contains 10 mg of doxorubicin Hydrochloride and 50 mg of lactose U.S.P. as a sterile red-orange lyophilized powder. Packaged and supplied in 10-vial cartons NDC 36242-814-10.

25 mg—Each rubber disc-capped vial contains 25 mg of doxorubicin Hydrochloride and 125 mg of lactose U.S.P. as a sterile red-orange lyophilized powder. Packaged and supplied in a single-vial carton NDC 36242-875-50.

Revised 9/75

* Distributed by Adriamycin Laboratories Inc.
1995 Market Street
Wilmington, Delaware 19899

Manufactured by Farmilab S.p.A. – Italy
Aqueous Solution
LIQUAEMIN SODIUM
Heparin Sodium Injection USP
heparin you can depend on both for service and for quality

Available in:
LIQUAEMIN SODIUM “10” Aqueous Solution 1,000 USP units/cc—10-cc and 30-cc vials.
LIQUAEMIN SODIUM “50” Aqueous Solution 5,000 USP units/cc—1-cc and 10-cc vials; 1-cc ampuls.
LIQUAEMIN SODIUM “100” Aqueous Solution 10,000 USP units/cc—1-cc and 4-cc vials; 1-cc ampuls.
LIQUAEMIN SODIUM “200” Aqueous Solution (not isotonic) 20,000 USP units/cc—1-cc, 2-cc, 5-cc and 10-cc vials; 1-cc ampuls.
LIQUAEMIN SODIUM “400” Aqueous Solution (not isotonic) 40,000 USP units/cc—1-cc and 5-cc vials.

Organon Pharmaceuticals
A Division of Organon Inc.
West Orange, N.J. 07052
Take a tip from Kormed.

A tip for consistently undistorted bone and marrow samples -- with the Jamshidi needle.

The Jamshidi Bone and Marrow Biopsy-Aspiration Needle, featuring an exclusive tapered needle tip, has been proven to be superior in obtaining undistorted bone and marrow samples with unaltered, well-preserved architecture. Designed for the bone and marrow biopsy technique, the Jamshidi needle may be used to obtain simultaneity aspiration and bone and marrow biopsy specimens. These features combine to increase the probability of discovering significant pathology.

The unique design of the Jamshidi needle makes it the simplest, most effective instrument in use today. Its tapered distal portion allows the tissue to freely enter the lumen of the needle, which avoids crushing of the tissue and plugging or impaction of marrow in the lumen -- the major limitations of most bone and marrow biopsy instruments. The distal tip is beveled and has a sharp, long-lasting cutting edge, which is designed to be easily resharpened when necessary.

The proximal end of the needle will accept any standard Luer-tip syringe to facilitate aspiration. The needle is fitted with a sharp inner stylet, which is designed to interlock into the needle and project just beyond the tapered distal portion to protect the cutting edge.

The stylet is removed upon entering the marrow cavity.

The probe is used to remove the biopsy specimen by introduction through the distal, or cutting, end of the needle.

The Jamshidi Bone and Marrow Biopsy-Aspiration Needle is available in the following different sizes:

<table>
<thead>
<tr>
<th>Pediatric</th>
<th>Orthopedic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant . . . 2 inch, 13 gauge</td>
<td>6 inch, 8 gauge</td>
</tr>
<tr>
<td>Pediatric . . . 3½ inch, 13 gauge</td>
<td>6 inch, 10 gauge</td>
</tr>
<tr>
<td>Adult . . . . 4 inch, 8 gauge</td>
<td>6 inch, 11 gauge</td>
</tr>
<tr>
<td>Regular . . . 4 inch, 11 gauge</td>
<td>Adult</td>
</tr>
</tbody>
</table>

For more information, call Kormed collect today at (612) 854-0300, write to the address below, or ask your medical supply dealer.
Blenoxane®
(sterile bleomycin sulfate)

An effective palliative agent in the management of the following neoplasms:

1/ selected squamous cell carcinomas
2/ selected lymphomas
3/ selected testicular carcinomas

...without clinically significant myelosuppression or immunosuppression.

The absence of toxic effects on the hematopoietic system and of any immunosuppressive action is emphasized, as this gives the drug a special importance.

...but dose-related pulmonary toxicity and frequent dermatological side effects:

Studies indicate that Blenoxane has significant toxicities. Pneumonitis occurs in about 10% of patients and occasionally progresses to pulmonary fibrosis even when detected in its early stages. Approximately 1% of patients treated have died of pulmonary fibrosis.

In addition, approximately half of the patients will exhibit some dermatological manifestations of therapy with Blenoxane. The skin reactions are usually characterized by erythema or hyperkeratosis, most often on the hands or elbows, which occasionally progress to ulceration.

The clinical use of Blenoxane requires a thorough knowledge of its activity, pharmacology, and toxicity—subjects which cannot be adequately reviewed in a communication of this type. We, therefore, urge those physicians who anticipate a use for Blenoxane to consult the Bristol Laboratories Blenoxane Monograph, available by mail from Bristol Laboratories or through your Bristol Representative.


Please see next page for Prescribing Information.
Blenoxane® (sterile bleomycin sulfate)

Brief Summary of Prescribing Information (2) 9/17/75
BLENNOXANE® (sterile bleomycin sulfate)
For complete information consult Official Package Circular.

Warning. It is recommended that Blenoxane be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.

Pulmonary fibrosis is the most severe toxicity associated with Blenoxane. The most frequent presentation is pneumonitis occasionally progressing to pulmonary fibrosis. Its occurrence is higher in elderly patients and in those receiving greater than 400 units total dose, but pulmonary toxicity has been observed in young patients and those treated with low dose.

A severe idiopathic reaction consisting of hypotension, mental confusion, fever, chills and wheezing has been reported in approximately 1% of lymphoma patients treated with Blenoxane.

Indications. Blenoxane should be considered a palliative treatment. It has been shown to be useful in the management of the following neoplasms either as a single agent or in proven combinations with other approved chemotherapeutic agents:

Squamous Cell Carcinoma: head and neck including mouth, tongue, tonsil, nasopharynx, oropharynx, sinus, palate, lip, buccal mucosa, gingiva, epiglottis; skin; larynx; penis; cervix and vulva. The response to Blenoxane is poorer in patients with head and neck cancer previously irradiated.

Lymphomas: Hodgkin’s, reticulum cell sarcoma, lymphosarcoma.

Testicular Carcinoma: embryonal cell, choriocarcinoma, and teratocarcinoma.

Contraindications. Blenoxane is contraindicated in patients who have demonstrated a hypersensitive or an idiopathic reaction to it.

Warnings. Patients receiving Blenoxane (sterile bleomycin sulfate) must be observed carefully and frequently during and after therapy. It should be used with extreme caution in patients with significant impairment of renal function or compromised pulmonary function.

Pulmonary toxicities occur in 10% of treated patients. In approximately 1%, the nonspecific pneumonitis induced by Blenoxane progresses to pulmonary fibrosis, and death. Although this is age and dose related, the toxicity is unpredictable. Frequent pulmonary function tests are recommended.

Idiopathic reactions similar to anaphylaxis have been reported in 1% of lymphoma patients treated with Blenoxane. Since these usually occur after the first or second dose, careful monitoring is essential after these doses.

Renal or hepatic toxicity, beginning as a deterioration in renal or liver function tests, have been reported, infrequently. These toxicities may occur, however, at any time after initiation of therapy.

Usage in Pregnancy: Safe use of Blenoxane in pregnant women has not been established.

Adverse Reactions. Pulmonary—This is potentially the most serious side effect, occurring in approximately 10% of treated patients. The most frequent presentation is pneumonitis occasionally progressing to pulmonary fibrosis. Approximately 1% of patients treated have died of pulmonary fibrosis. Pulmonary toxicity is both dose and age related, being more common in patients over 70 years of age and in those receiving over 400 units total dose. This toxicity, however, is unpredictable and has been seen occasionally in young patients receiving low doses.

Because of lack of specificity of the clinical syndrome, the identification of patients with pulmonary toxicity due to Blenoxane has been extremely difficult. The earliest symptom associated with Blenoxane pulmonary toxicity is dyspnea. The earliest sign is fine rales.

Radiographically, Blenoxane-induced pneumonitis produces nonspecific patchy opacities, usually of the lower lung fields. The most common changes in pulmonary function tests are a decrease in total lung volume and a decrease in vital capacity. However, these changes are not predictive of the development of pulmonary fibrosis.

The microscopic tissue changes due to Blenoxane (sterile bleomycin sulfate) toxicity include bronchioral squamous metaplasia, reactive macrophages, atypical alveolar epithelial cells, fibrinous edema, and interstitial fibrosis. The acute stage may involve capillary changes and subsequent fibrinous exudation into alveoli producing a change similar to hyaline membrane formation and progressing to a diffuse interstitial fibrosis resembling the Hamman-Rich syndrome. These microscopic findings are nonspecific, e.g., similar changes are seen in radiation pneumonitis, pneumocystic pneumonitis.

To monitor the onset of pulmonary toxicity, roentgenograms of the chest should be taken every 1 to 2 weeks. If pulmonary changes are noted, treatment should be discontinued until it can be determined if they are drug related. It has been suggested that treatment of Blenoxane-induced pneumonitis with corticosteroids may prevent progression to pulmonary fibrosis.

Idiopathic Reactions—In approximately 1% of the lymphoma patients treated with Blenoxane an idiopathic reaction, similar to anaphylaxis clinically, has been reported. The reaction may be immediate or delayed for several hours, and usually occurs after the first or second dose. It consists of hypotension, mental confusion, fever, chills, and wheezing. Treatment is symptomatic including volume expansion, pressor agents, antihistamines and corticosteroids.

Integument and Mucous Membranes—These are the most frequent side effects, being reported in approximately 50% of treated patients. These consist of erythema, rash, urticaria, vesication, hyperpigmentation, and tenderness of the skin. Hyperkeratosis, nail changes, alopecia, pruritus, and stomatitis have also been reported. It was necessary to discontinue Blenoxane therapy in 2% of treated patients because of these toxicities.

Skin toxicity is a relatively late manifestation usually developing in the 2nd and 3rd week of treatment after 150 to 200 units of Blenoxane has been administered and appears to be related to the cumulative dose.

Other—Fever, chills, and vomiting were frequently reported side effects. Anorexia and weight loss are common and may persist long after termination of this medication. Pain at tumor site, phlebitis, and other local reactions were reported infrequently.

Dosage. Because of the possibility of an anaphylactoid reaction, lymphoma patients should be treated with 2 units or less for the first 2 doses. If no acute reaction occurs, then the regular dosage schedule may be followed.

The following dose schedule is recommended: Squamous cell carcinoma, lymphosarcoma, reticulum cell sarcoma, testicular carcinoma—0.25 to 0.50 units/kg. (10 to 20 units/M2) given intravenously, intramuscularly or subcutaneously weekly or twice weekly.

Hodgkin’s Disease—0.25 to 0.50 units/kg. (10 to 20 units/M2) given intravenously, intramuscularly or subcutaneously weekly or twice weekly. After a 50% response, a maintenance dose of 1 unit daily or 5 units weekly intravenously or intramuscularly should be given.

Pulmonary toxicity of Blenoxane appears to be dose-related with a striking increase when the total dose is over 400 units. Total doses over 400 units should be given with great caution.

Note: When Blenoxane is used in combination with other antineoplastic agents, pulmonary toxicities may occur at lower doses.

Improvement of Hodgkin’s disease and testicular tumors is prompt and noted within two weeks. If improvement is seen by this time, improvement is unlikely. Squamous cell cancers respond more slowly, sometimes requiring as long as three weeks before any improvement is noted.

Supply. Each ampule contains 15 units of Blenoxane as bleomycin sulfate.

For administration and more complete information, consult package circular.
AMERICAN JOURNAL OF HEMATOLOGY
a new journal covering a broad range of hematological topics in clinical and basic research

CONTENTS • VOLUME 1, NUMBER 2 • APRIL, 1976

A Prophylactic Transfusion Program for Children with Sickle Cell Anemia Complicated by CNS Infarction, Jeanne M. Lusher, Hushang Haghlighat, and A. Samy Khalifa

ABO Hemolytic Disease of Newborn, Without Hyperbilirubinemia, Eugene Kaplan, Fritz Herz, and Else Scheyes


Chemotherapy of Acute Lymphoblastic Leukemia in Children, Mahroo Hagbin

The Human Spleen as Revealed by Scanning Electron Microscopy, Marion I. Barnhart and Jeanne M. Lusher

T and B Lymphocytes in Leukemia Therapy, Elaine Estes, William DiNicolos, Nasser Movassaghi, and Sanford Leikin

Red Cell Values on the First Postnatal Day During the Last 16 Weeks of Gestation, Rina Zaitov and Yehuda Matot

Identification of T Cell Lymphoma Tumor Antigens on Human T Cell Lines, Joseph Kaplan


Identification of Cells in Culture, C. S. Stulberg, W. D. Peterson, Jr., and W. F. Simpson

EDITOR

Ananda S. Prasad
Wayne State University School of Medicine, 540 East Canfield Street, Detroit, Michigan 48201

ASSOCIATE EDITORS

Richard H. Aster, Milwaukee Blood Center, Inc.
Carter R. Bishop, Wayne State Univ. School of Medicine
George J. Brewer, Univ. of Michigan Medical School
Kurt Hirschhorn, Mount Sinai School of Medicine
Eberhard F. Mammen, Wayne State Univ. School of Medicine
Wendell F. Rosse, Duke Univ. Medical Center
Kouichi R. Tanaka, Harbor General Hospital

EDITORIAL BOARD

Martin J. Cline, UCLA School of Medicine
Marcel Conrad, Univ. of Alabama Medical School
Daniel Deykin, VA Hospital, Boston
Jochen Duhm, Universität München
Eloise R. Giblett, King County Central Blood Bank, Seattle
Donald R. Harkness, VA Hospital, Miami
Titus H. J. Huisman, Medical College of Georgia
Harold M. Maurer, Medical College of Virginia
Shiro Miwa, Yamaguchi Univ. School of Medicine
B. P. L. Moore, Nat'l. Reference Laboratory (W.H.O.)
Herbert Perkins, San Francisco Medical Society
Judith G. Pool, Stanford Univ. Medical Center
Noel R. Rose, Wayne State Univ. School of Medicine
Luigi Ross-Bernardi, University of Milan
Robert F. Schilling, University of Wisconsin
Robert Silber, NYU School of Medicine
Louis W. Sullivan, Morehouse College, Atlanta
Douglas MacN. Surgeon, SUNY, Buffalo

also available

ERYTHROCYTE STRUCTURE AND FUNCTION

Just Published
Proceedings of the Third International Conference on Red Cell Metabolism and Function, October, 1974
George Brewer, Editor 784 pp. $48.00

TRACE COMPONENTS OF PLASMA: Isolation and Clinical Significance

January 1976
G. A. Jamieson and Tibor J. Greenwalt, Editors 450 pp. $37.50

AMERICAN JOURNAL OF HEMATOLOGY

Volume 1, 1976, Quarterly
$35.00 per volume ($2.00 additional postage outside U. S.)
Please enclose payment with order

published by

Alan R. Liss, Inc.
150 Fifth Ave.
New York, N.Y. 10011
Q. Automate Differentials? Why? And why go with Technicon?
A. You automate for four basic reasons...

...You hope to (1) improve precision, (2) improve accuracy, (3) increase productivity, and (4) provide better patient care. For the money you'll spend to automate diffs, you should expect to get all four benefits.

Q. But why Technicon's Hemalog D? Aren't these benefits available on other systems?

A. No. Let me explain. Basically, there are two types of systems to choose from: the Hemalog D continuous-flow system, which cytochemically classifies and counts 10,000 cells for each sample at an analytical rate of up to 60 samples per hour; and pattern-recognition instruments, which link a computer to a microscope and manually classify and count 100 cells at rates of 25-40 samples/hour.

Q. What does this have to do with the benefits you listed?

A. Take precision. Since precision varies with the square root of the number of cells counted, a 10,000-cell count is ten times more precise than a 100-cell count. This results in fewer misses on numerically marginal abnormal diffs. A more precise count also gives a better indication of changes in patient status. This is important if the physician ever hopes to use day-to-day changes in the rarer cell types (eos, basos, monos) to monitor patients. As one pathologist said, "The 100-cell differential is dead. Linking a computer to it is like putting an air conditioner in a covered wagon."

Q. And accuracy?

A. The Hemalog D accurately identifies each normal mature cell type by the presence or absence of specific peroxidase and esterase enzymes and heparin. Abnormal samples are flagged for microscopic review. The cell lines of the large mature and immature mono-nuclear cells, often confusing because of their similar morphology, are easily distinguished on the basis of their biochemical characteristics.

Q. You haven't said much about productivity or cost-effectiveness.

A. The Hemalog D sampler accepts EDTA anticoagulated whole blood. After loading the samples, operation from sampling to printout is completely unattended. Pattern-recognition systems require a number of operator interventions on every normal sample. As for cost effectiveness, you see a lot of figure juggling, but many of the larger private labs, where costs are critical, have acquired Hemalog D's. One has even dropped the price of the diff as a result.

Q. I've heard that the speed of the D is negated by having to review up to 50% of the samples.

A. Not so. At one university center, which has a large percentage of abnormal hematologic cases, 30% of the samples require microscopic reviews. On the other hand, a number of general hospitals required reviews on only 15% of their patients. When five labs did double-blind arbitration studies comparing the Hemalog D with the 100-cell manual count, they found that significantly fewer abnormal cases were missed by the Hemalog D. Since accuracy of screening is highly dependent on precision, 100-cell pattern-recognition systems will be hard put to prove that they provide more accurate screening than manual techniques.

Q. I agree that superior precision and accuracy should help my patients. Is that all you mean by 'better patient care'? That sounds like advertising jargon.

A. Let me be specific. I'm talking about four additional benefits, each of which can contribute to better patient care:

(1) Absolute Numbers. Hematologists try to think in terms of absolute values. The Hemalog D prints out absolute numbers (cells/mm³) and percentages on the report form, permitting more direct interpretations of the numerical results, e.g., differentiating a neutrophilia and lymphopenia.

(2) Precise Monitoring of Patient Status. With enhanced precision, small changes in differentials become statistically significant; this allows for the dynamic tracking of patients undergoing therapy.

(3) Differential Counts When the Total Count is as Low as 400 cells/mm³. This capability allows the clinician to monitor, for example, the course of chemotherapy in leukemia patients with much greater reliability.

(4) More Time to Spend on Abnormals. Hemalog D rapidly identifies the abnormals. This frees the staff to give greater care and attention to the abnormal blood smears.

Technicon Hemalog D
INFORMATION FOR CONTRIBUTORS

SUBMITTING THE MANUSCRIPT

BLOOD, The Journal of the American Society of Hematology, provides an international forum for the publication of original articles describing basic laboratory and clinical investigations encompassed in the broad discipline of hematology. The scope of the journal covers all aspects of hematology, including disorders of leukocytes, both benign and malignant, erythrocytes, platelets, hemostatic mechanisms, and immunology, as well as major developments in clinical laboratory diagnosis and blood banking.

Manuscripts are accepted for consideration on the condition that they are contributed solely to BLOOD. No substantial part of a paper may have been or may be published elsewhere, except for an abstract of 500 words or less. Manuscripts will be critically reviewed by the Editor, the appropriate Associate Editor, and other independent referees. Acceptance of papers for publication is based on the originality of the observation or investigation, the quality of the work described, and the clarity of the presentation. Papers will ordinarily be published in the order in which they are finally accepted for publication and not in the order of submission.

Acknowledgments to other investigators for advice, assistance, and data must be substantiated by written authorization to the Editor-in-Chief specifically granting permission to the authors for such citations.

Letters to the Editor: Letters to the Editor are welcomed and will be published if appropriate. They should be typewritten, double spaced, and, generally, should not be more than two typewritten pages in length.

Editorials, Brief Reviews: Editorials and Brief Reviews may be solicited by the Editors, and may be submitted for consideration without solicitation. These manuscripts must be prepared in a manner appropriate for any other papers and will be reviewed as are original articles submitted for consideration.

Articles, editorials, letters to the editor, and other text material in BLOOD represent the opinions of the authors and do not reflect the opinions of the American Society of Hematology, the publisher, or the institution with which the author is affiliated, unless the contrary is clearly specified.

Manuscripts and all communications concerning editorial matters should be addressed to the Editor-in-Chief, Dr. Ernst R. Jaffe, Albert Einstein College of Medicine of Yeshiva University, 1300 Morris Park Avenue, Bronx, New York 10461, telephone (212) 430-4040.

Papers reporting human experimentation will be reviewed in accordance with the precepts established by the Helsinki Declaration. Copies of this declaration may be obtained by writing to the American Medical Association, 535 North Dearborn Street, Chicago, Illinois. Such papers must include a statement that the human investigations were performed after approval by a local Human Investigations Committee and in accord with an assurance filed with and approved by the Department of Health, Education, and Welfare where appropriate.

PREPARING THE MANUSCRIPT

Manuscripts must be typewritten, double or triple-spaced on good quality 8½-by-11-inch white paper with margins of at least one inch. Please do not use erasable bond. The original and two complete copies of the manuscript must be submitted.

The first page of the manuscript should contain the following information: (1) title of the paper; (2) authors' names; (3) name of institution in which work was done; (4) acknowledgments for research support; (5) name and address of the author to whom communications regarding the manuscript should be directed.

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.

(Continued on page xxii)
An easy, reliable, routine screening test that provides rapid FDP determinations "around-the-clock."

Thrombo-Wellcotest®

Simple, sensitive, reliable...and fast: A latex slide test for Fibrinogen Degradation Products or fibrin related antigens that screens both urine and serum STAT.

No need for special training: Night and weekend testing can be performed routinely.

Sensitive: Detects fibrin monomers and all four fragments — X, Y, D and E.

Reliable: correlates well with tanned red cell hemagglutination-inhibition immunoassay and "staph-clumping" test.1,2,3

Semi-quantitative assays: gives FDP levels in 3 breakdowns: less than 10 μg/ml, between 10 and 40 μg/ml and over 40 μg/ml.

Relatively inexpensive: can be performed on single sera without wasted reagents.

Complete: no additional reagents needed; all you supply is the test tubes.


and for more quantitative analysis

The Wellcome® FDP Kit

Convenient, compact, classical tanned red cell hemagglutination-inhibition assay complete—all you supply is microtitration equipment.

From serum to endpoint in minutes


(Continued from page xx)

**PREPARING ILLUSTRATIONS AND TABLES**

Tables and illustrations must be cited in order in the text using arabic numerals. All line drawings should be submitted as clear, glossy, black and white photographs. Legible copies may be used with the duplicate manuscript. Photomicrographs and other photographic illustrations must be submitted in duplicate; copies are not acceptable. Legends for illustrations should be typewritten, double-spaced, on a separate sheet, and included at the end of the manuscript. A legend must accompany each illustration. Contributors will pay all charges involved in processing and printing of color photographs.

Each table should be typed on a separate sheet and appropriately numbered. Legends should be typed on the same sheets as the tables. Tables in excess of one and one-half printed pages may be charged for at approximately $80.00 per page.

**REFERENCES**

References should be compiled at the end of the article according to the order of citation in the text. They should be typewritten, double-spaced under the heading REFERENCES. Abbreviations for titles of medical periodicals should conform to those used in the latest edition of Index Medicus. (A "List of Journals Indexed in Index Medicus"—with abbreviations—is obtainable from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, at a modest charge.)

Personal communications and references to publications in press by authors other than those submitting the paper must be substantiated by a letter from the investigator(s) concerned confirming the data or observations and granting the authors permission to cite the material.

**EXAMPLES OF REFERENCES**

Journal article, one author:


Journal article, two or more authors:


Journal article, in press:


Complete book:


Chapter of book:


Chapter of book that is part of published meeting:


Chapter of book that is part of unpublished meeting:


**PROOFREADING**

Contributors are provided with galley proofs and are asked to proofread them for typesetting errors. Important changes in data are allowed, but authors will be charged for excessive alterations in proof. Galley proofs should be returned within 48 hours.

(Continued on page xxiii)
REPRINTS

Reprints of articles will be furnished to contributors when ordered in advance of publication. An order form, showing cost of reprints, is sent with proofs. Individuals wishing to obtain reprints of an article that appeared in BLOOD can do so by contacting the author at the address given in the journal.

ANNOUNCEMENTS

Announcements of meetings, conferences, and the like which are of interest to the readership of BLOOD should be sent to the Editor at least three months before the first day of the month of issue. These items should be as concise as possible. When considered appropriate, they will be published as promptly as possible, subject to the availability of space in the journal.

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 x 10^12/l*</td>
</tr>
<tr>
<td>PCV</td>
<td>0.41*†</td>
</tr>
<tr>
<td>MCV</td>
<td>75–95 fl§</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 x 10^9/l</td>
</tr>
<tr>
<td>Platelets</td>
<td>150–400 x 10^9/l</td>
</tr>
<tr>
<td>Red cell diameter</td>
<td>6.7–7.7 μm</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>0.2–2.0%</td>
</tr>
<tr>
<td>Serum iron</td>
<td>14–29 μmol/l§</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>45–72 μmol/l¶</td>
</tr>
<tr>
<td>Transferrin</td>
<td>1.2–2.0 g/l</td>
</tr>
<tr>
<td>Serum haptoglobins</td>
<td>0.3–2.0 g/l</td>
</tr>
<tr>
<td>(Hb binding)</td>
<td></td>
</tr>
<tr>
<td>Serum B12</td>
<td>160–925 ng/l</td>
</tr>
<tr>
<td>(as cyanocobalamin equivalents)</td>
<td></td>
</tr>
<tr>
<td>Serum folate</td>
<td>2–20 μg/l</td>
</tr>
<tr>
<td>Plasma fibrinogen</td>
<td>1.5–4.0 g/l</td>
</tr>
</tbody>
</table>

* As the normal range varies with age and sex, only one measurement in the normal range has been given as an example.
† dl, deciliter.
§ fl = femtoliter.
¶ Calculated from the molecular weight of iron (55.95).

**125I METHOTREXATE*–RIA KIT**

The "stat" radioimmunoassay for the measurement of circulating methotrexate utilizes an 125I methotrexate derivative of high specific activity, allowing quantitation of from 150 pg to 15 ng. Incubation time is 30 minutes using a precise double antibody technique. Crossreactivity of the antiserum against most folate analogues (including Nf-methyl-tetrahydrofolic acid and folic acid) is less than 0.1%. The methotrexate derivative has been shown to bind to the enzyme dihydrofolate reductase; "in vitro," as does methotrexate itself. The kit contains all reagents necessary for 100 tubes.

Diagnostic Biochemistry
Inc
10457-H ROSELLE STREET • SAN DIEGO, CA 92121 • (714) 452-0950

*Patent applied for.
Test Serums
Serological Reagents
from BIOTEST

Reliability Creates Confidence