INDEX TO ADVERTISERS
APRIL 1975

From Adria Laboratories

an anticancer compound
with a wide range of activity

Adriamycin™
(doxorubicin HCl)
for injection
10 mg
FOR INTRAVENOUS USE ONLY

produces significant regression in a number of solid tumors, as well as remissions in certain hematologic malignancies

Adriamycin has proved active against such neoplastic conditions as: acute lymphoblastic leukemia, acute myeloblastic leukemia, Wilms' tumor, soft tissue and osteogenic sarcoma, neuroblastoma, breast carcinoma, ovarian carcinoma, transitional cell bladder tumor, bronchogenic lung carcinoma, thyroid carcinoma, lymphoma of both Hodgkin and non-Hodgkin type.

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.

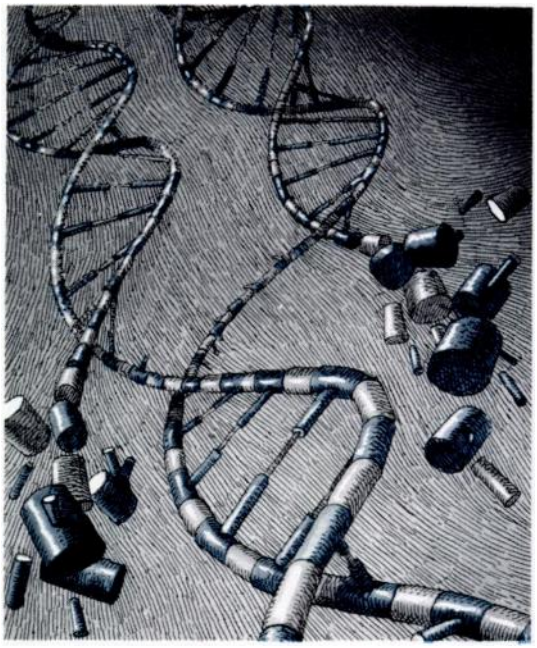
The incidence of bone marrow depression is high. Hematopoietic toxicity may limit dosage.

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

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

For consultation on the use of Adriamycin, call collect **(302) 575-7830** at any time of the day or night.

For complete prescribing information, please see the facing page.



Artist's conception of DNA replication.
Adriamycin is thought to produce its antineoplastic effect by inhibiting the synthesis of DNA and RNA. This inhibition may be due to the binding of Adriamycin to DNA.

ADRIAMYCIN (doxorubicin HCl) for injection.
FOR INTRAVENOUS USE ONLY

WARNINGS

1. Severe local tissue necrosis will occur if there is extravasation during administration.
2. Serious irreversible myocardial toxicity with delayed congestive failure unresponsive to any cardiac supportive therapy may be encountered as total dosage approaches 550 mg/M².
3. Dosage should be reduced in patients with impaired hepatic and renal function.

DESCRIPTION

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

CLINICAL PHARMACOLOGY

Pharmacologic studies after the intravenous administration of radiolabeled Adriamycin (Doxorubicin Hydrochloride for Injection) indicate rapid plasma clearance of a significant portion of the administered drug and slow excretion in urine and bile, suggesting significant tissue binding. Plasma levels of radioactivity were about ½ initial levels in 30 minutes and remain fairly constant for seven to ten days at least. Urinary excretion ranges from 25% to 35% in seven days. Fecal excretion ranges from 15% to 45% in seven days. The site of Adriamycin activity is thought to be at the level of DNA and RNA synthesis. Cell culture studies have demonstrated rapid cell penetration and perinucleolar chromatic binding.

INDICATIONS

Adriamycin should be used under the direction of specialists qualified in the administration of cytotoxic drugs. Adriamycin has been used successfully to produce regression in neoplastic conditions such as: acute lymphoblastic leukemia, acute myeloblastic leukemia, Wilms' tumor, soft tissue and osteogenic sarcoma, neuroblastoma, breast carcinoma, ovarian carcinoma, transitional cell bladder tumor, bronchiogenic lung carcinoma, thyroid carcinoma and lymphoma of both Hodgkin and non-Hodgkin types. A number of other solid tumors in the pediatric age group have also shown some responsiveness but in numbers too limited to justify specific recommendation.

CONTRAINDICATIONS

Adriamycin therapy should not be started in patients who have myelosuppression induced by previous treatment with other antiblastic agents or in patients with impaired cardiac function (see Precautions).

WARNINGS

There is a high incidence of bone marrow depression, primarily of leukocytes, which requires careful monitoring of white blood cell levels. Red blood cell and platelet levels should also be monitored since they may also be depressed. Hematopoietic toxicity may require suspension or cessation of Adriamycin therapy.

The total dose of Adriamycin administered to the individual patient should also take into consideration any previous therapy with related tetracyclic compounds such as Daunomycin (Daunorubicin).

Prior to the initial dosing, evaluation of hepatic function is recommended using conventional clinical laboratory tests such as SGOT, SGPT, alkaline phosphatase, bilirubin, and BSP. Initial treatment with Adriamycin requires close observation of the patient and extensive laboratory monitoring. It is recommended that patients should be hospitalized at least during the first phase of the treatment. There is no adequate information on whether this drug may affect fertility in human males or females or have a teratogenic potential or other adverse effect on the fetus. Adriamycin and related compounds have been shown to have carcinogenic properties when tested in experimental animals.

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 anti-infective agent.

PRECAUTIONS

Special attention must be devoted to the cardiotoxicity exhibited by Adriamycin. Although uncommon, acute left ventricular failure has occurred particularly in patients who have received total dosage of the drug exceeding the currently recommended limit of 550 mg/square meter of body surface. The cardiac failure often occurs several weeks after administration of the drug and is not favorably affected by the presently known medical or physical therapy for cardiac support. Baseline EKG and a monthly followup EKG is recommended during and immediately following active drug therapy. EKG changes such as T-wave flattening, S-T depression, voltage reduction, and arrhythmias may serve as indications for suspension of Adriamycin therapy; although it must be recognized that fatal cardiotoxicity can occur precipitously without antecedent EKG alterations.

ADVERSE REACTIONS

Complete alopecia almost uniformly accompanies therapy, and patients should be advised of this normal consequence of treatment.

Stomatitis and esophagitis are common. These effects may be quite severe, leading to ulceration.

Gastrointestinal symptoms including nausea, vomiting, and diarrhea may occasionally occur. Hyperpigmentation of nailbeds and dermal creases may occur in children. Severe cellulitis, vesication, and tissue necrosis result if Adriamycin is extravasated during administration.

DOSAGE & ADMINISTRATION

The recommended dosage schedule for adults is 60 to 75 mg/square meter of body surface as a single intravenous injection administered at 21-day intervals. An alternative dosage schedule, preferred in pediatric therapy, is 30 mg/square meter in a single intravenous dosage on three successive days repeated every four weeks.

A dose level of 40-55 mg/square meter at each administration is recommended if hepatic function is impaired. Toxicity in patients with renal pathology is inconsistent so that dosage must be carefully monitored.

Each vial of Adriamycin contains ten (10) mg of freeze-dried Doxorubicin Hydrochloride. Its contents should be reconstituted and dissolved in five (5) ml of Sodium Chloride Injection U.S.P. After reconstitution, the product may be stored for twenty-four (24) hours at room temperature or forty-eight (48) hours if refrigerated (4-10° C). It should be protected from exposure to sunlight. It is recommended that Adriamycin be administered into the tubing of a freely running intravenous infusion of normal saline or five percent (5%) dextrose. This procedure will reduce likelihood of extravasation and consequent tissue damage.

Adriamycin has been used in combination with other approved cancer chemotherapeutic agents; however, the benefits or risks of such therapy have not been fully elucidated.

HOW SUPPLIED

Each rubber disc-capped vial of Adriamycin contains 10 mg of Doxorubicin Hydrochloride and 50 mg of lactose U.S.P. as a red-orange lyophilized powder.
Package 10 vials.

Adria
Distributed by Adria Laboratories, Inc.
1105 Market Street,
Wilmington, Delaware 19801.
Manufactured by: Farmitalia, Milan, Italy.

Enter the new era in automated cell counting where accuracy and precision cost less.
An application of laser particle-counting, Hemac 630L reconciles economy of operation with sophisticated technology. Hemac aspirates only 90 microliters (approximately) of whole blood. Reagent consumption for a 7 parameter CBC is thus cut to less than 14 ml, including diluent. And 14 ml translates to 3 cents in reagent cost per test.

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Hemac requires little from the operator in return for trouble-free performance.
Once automatic sample aspiration is initiated through insertion of printout card and positioning of specimen (by moving a lever), the probe is automatically cleansed, internally and externally. Stable electronics (miniaturized integrated circuits) minimize downtime and extended working range means fewer dilutions and repeat runs. Access to parts subject to routine maintenance is simple and instantaneous.

Easily adapted to your present laboratory system.
Low start up and maintenance time and sample throughput of 60 per hour make Hemac an asset to a considerable range of test volumes. Hemac can be ready for samples on a 24 hour basis. Venous or capillary whole blood may be used. Installation requires only a 115 V., 8 ampere power source. Serial ASCII output is available for computer or teletype compatibility.

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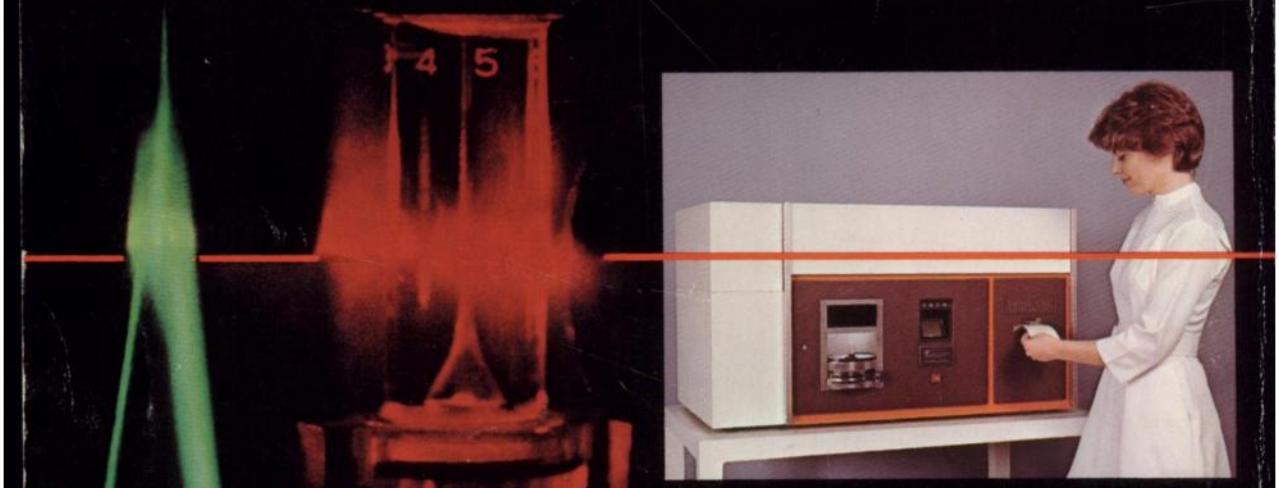
LASER HEMATOLOGY COUNTER



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