

propriate therefore, to use urinary volume as the prime determinant in considering a patient for dialysis. Another important consideration regarding the duration of survival after initial dialysis is the presence or absence of potentially reversible conditions aggravating uremia. Those patients who survived more than three months had a higher proportion of reversible conditions present than those surviving less than three months ($P < 0.01$).

There are also certain clinical situations in which peritoneal dialysis should be considered in the treatment of patients having chronic renal failure. A small group of patients may have surgically correctable lesions; dialysis may alleviate uremic symptoms and permit surgery. Some patients with chronic renal disease may become more uremic as a result of intercurrent infection, surgery, or trauma. These individuals may be maintained with dialysis while the complicating process is treated. A reasonably compensated state compatible with many months of productive life may be reestablished. Dramatic relief of uremic symptoms, often of some duration, may be obtained in certain patients with slowly progressive renal failure. In such patients the use of dialysis instead of conservative medical measures may shorten the duration of hospitalization.

It is frequently impossible to determine on initial examination if a patient has acute or chronic renal failure, especially when past medical history is lacking. In these situations, dialysis is justified to maintain the patient's life while appropriate studies are carried out to determine the nature of the renal lesion.

It is important to understand precisely what dialysis accomplishes. It does not improve renal function or alter the course of renal disease. It does, however, relieve the symptoms of uremia. It gains survival time for the patient so that medical or surgical therapy may be instituted. Complications which frequently co-exist with chronic renal insufficiency may be partially or completely alleviated during the time gained by peritoneal dialysis. These complications include exacerbations of glomerulonephritis or urinary tract infection, urinary tract obstruction, hypertensive crises, congestive heart failure, trauma, systemic infection, or other disease processes. In this manner patients with an apparently hopeless prognosis may be salvaged.

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Androgenic Hormone Therapy in Lymphatic Leukemia

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ANEMIA may occur during the course of chronic lymphatic leukemia. The study of erythrokinetics has revealed that the development of this anemia may be due to decreased erythropoiesis with normal or increased red blood cell destruction or loss. There is little understanding of the reason for the failure of leukemic marrow to provide adequate erythropoiesis. A metabolic competition between developing red blood cells and pathological white cells has been suggested.¹ Because of the stimulation of erythropoiesis produced by androgenic hormones, androgens were administered to patients with lymphatic leukemia.

In patients with advanced breast cancer, androgenic hormones produced reticulocytosis, normoblastic hyperplasia of the bone marrow, and an increase in hemoglobin even to polycythemic values (Fig 1).^{2,3} Because of these observations, androgens were employed in the treatment of a variety of anemias.³⁻⁵ Improvements were noted in aplastic anemia, refractory anemia, myelofibrosis, and various diseases with erythroid hypoplasia. During a study of the effect of androgenic hormones in malignant diseases with depressed marrow function, a striking response in patients with chronic lymphatic leukemia was noted.

Materials

Androgenic hormones were administered to 12 patients with subacute or chronic lymphatic leukemia and anemia to improve the hematopoietic function of the bone marrow and as an adjuvant to cancer chemotherapy.

The androgenic hormones employed were fluoxymesterone, 20 to 50 mg orally per day, and testosterone enanthate, 400 to 1,800 mg per week intramuscularly in divided doses. A minimum period of effective therapy was regarded to be two months. Adrenal steroids were administered with the androgenic hormone because it has been observed that combined therapy appears to potentiate the stimulation of erythropoiesis.²

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Erythropoiesis-stimulating Effect of Androgenic Hormone Therapy in Seven of 12 Patients With Lymphatic Leukemia and Anemia.

Patient No.	Type of Lymphatic Leukemia	Therapy Prior to Androgen Treatment	Duration of Androgen Treatment, Mo	Duration of Improvement, Mo	Hemoglobin, Gm %		Platelets, 10 ³ /Cu Mm	
					Pre-treatment	Maximum Level	Pre-treatment	Maximum Level
1	Subacute	Irradiation Prednisone	6	8	5.5	16.7	138	176
2	Subacute	Prednisone	28+	24+	5.3	15.4	5	62
3	Chronic	Uracil mustard Irradiation	2	3	9.6	12.1	70	66
4	Chronic	Uracil mustard Irradiation Prednisone	6	6	8.7	13.7	32	174
5	Chronic	Irradiation Chlorambucil Prednisone	6+	6+	8.4	16.1	88	122
6	Chronic	Uracil mustard Prednisone	24+	24+	5.6	16.8	122	91
7	Chronic	Irradiation Prednisone	24+	24+	4.9	18.2	62	244

Results

Androgenic hormone was administered to nine patients with chronic lymphatic leukemia and three patients with subacute lymphatic leukemia. The major problem in all these patients was an anemia characterized by erythroid hypoplasia of the bone marrow. Hemolysis was excluded as a major cause of the anemia and adrenal steroids had not been effective in its treatment.

A striking increase in erythropoietic activity and a resultant increase in hemoglobin occurred in seven patients (Table). This increased activity resulted in reticulocytosis, an increase in hemoglobin, and a normoblastic hyperplasia of the bone marrow.

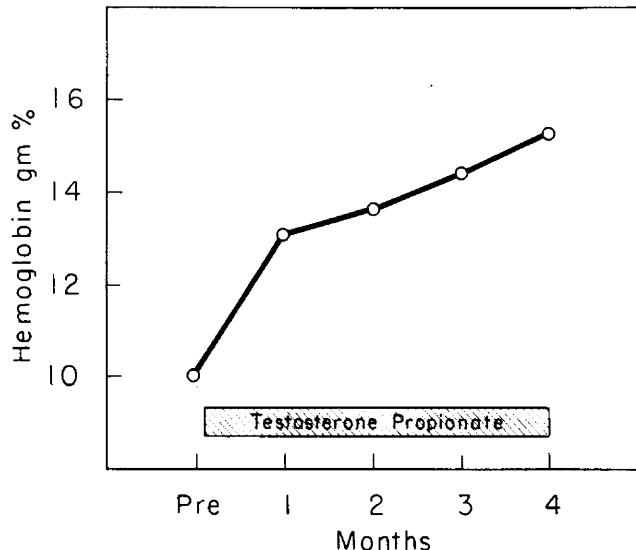
Report of a Case

A 44-year-old man had a carcinoma of the left testis removed in 1954. Surgery was followed by irradiation therapy. In 1959 a diagnosis of leukemia was established and repeated courses of irradiation therapy were administered. By January, 1962, there was marked anemia requiring repeated transfusions. In March, 1962, prednisone was begun with no effect.

The patient was first seen at the University of Minnesota Hospitals on April 2, 1962.

The patient was pale. There were enlarged nodes in the cervical, supraclavicular, axillary, and inguinal regions. There was slight hepatomegaly and splenomegaly. Roentgenograms revealed mediastinal and retroperitoneal nodes. The hemoglobin was 6.4 gm% and white blood cell (WBC) count, 10,950 cumm, with 18% neutrophils and 70% mature lymphocytes. The platelet count was 62,000/cu mm and less than 0.1% reticulocytes were present. A bone marrow aspiration could not obtain marrow material. A cervical lymph node biopsy and a rib biopsy revealed chronic lymphatic leukemia of the node, marrow, and muscle. The marrow count had 73.6% lymphocytes, 0.6% normoblasts, and 23.2% neutrophils. Stool urobilinogen value was 150 mg per day and the serum iron was 207 γ%. During the study the hemoglobin dropped to 4.9 gm%.

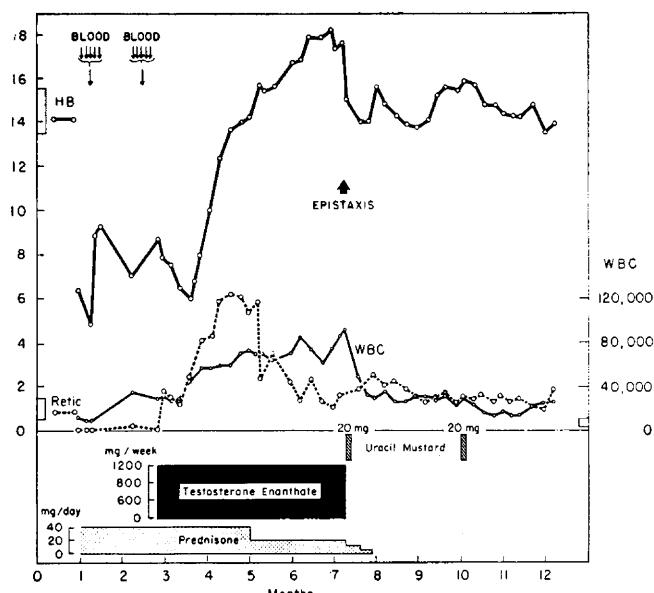
The course of the patient is demonstrated in Fig. 2. Blood transfusions were administered to maintain the hemoglobin above 8 gm%. Three months after prednisone therapy was begun there was no evidence of improvement. Therefore, testosterone enanthate therapy, 400 mg three times a week intramuscularly, was begun. There was an immediate reticulocytosis to a maximum level of 6.1%. The hemoglobin rapidly increased to a maximum level of 18.2 gm%. The WBC count slowly rose to 92,000/cu mm. A successful bone marrow aspiration revealed 10.8% normoblasts and 70% lymphocytes. After 4½ months of androgen therapy the patient developed a



1.—Stimulation of erythropoiesis by testosterone propionate in woman with advanced breast cancer.

severe epistaxis. The hemoglobin level fell to 14.0 gm%. Because this complication was apparently due to the polycythemia, the androgen and steroid therapy were discontinued. Because of the elevated WBC count, 20 mg of uracil mustard was administered orally for two days. A decrease in the leukocyte count occurred. A second course of uracil mustard three months later produced a further decrease of WBC's to a low of 13,400/cu mm. The hemoglobin level remained normal for six months after androgen therapy was discontinued. At that time the anemia recurred. Retreatment with testosterone enanthate, prednisone, and cyclophosphamide resulted in a second remission. The patient has continued to receive a maintenance dose of testosterone enanthate, 400 mg every three weeks, and prednisone, 10 mg daily. Two years after initiating androgen therapy the patient is well, with a normal WBC count and hemoglobin level. A bone marrow aspiration revealed 27.5% normoblasts and 65% lymphocytes.

The duration of androgen therapy was less than two months in five patients with chronic lymphatic leukemia and in one with subacute lymphatic leukemia. Of these, only one patient with chronic lymphatic leukemia had an improvement. In the other five patients, therapy was interrupted because of death due to intercurrent infection. In general, these patients had advanced leukemia.



2.—Effect of testosterone enanthate in 44-year-old patient with chronic lymphatic leukemia and erythroid hypoplasia of bone marrow.

Four patients with chronic lymphatic leukemia and two with subacute lymphatic leukemia were treated more than six months with androgenic hormone; all had a significant increase in erythroid activity (Table). The mean pretreatment level of hemoglobin was 6.9 gm% for the seven patients that improved. The mean of the maximum hemoglobin value was 15.6 gm%, or a mean increase of 8.7 gm%.

Four of the seven patients are still receiving androgen therapy, three for more than 24 months. Three patients who had increased erythroid activity died of intercurrent infection.

In all the patients, the initial platelet count was reduced, in some instances limiting the use of specific anti-leukemic therapy. During androgenic hormone administration, significant increases of the platelet count occurred in three patients also demonstrating an erythroid response (patients 2, 4, and 7), but in one of these the count did not approach normal levels (patient 2). There was no increase in platelet count in the five patients that failed to demonstrate an erythropoietic response.

Four patients with chronic lymphatic leukemia developed leucocytosis or lymphadenopathy after stimulation of erythropoiesis had been demonstrated. The administration of uracil mustard or cyclophosphamide resulted in an objective improvement in all these patients.

Comment

Androgenic hormone therapy was administered to 12 patients with subacute or chronic lymphatic leukemia characterized by erythroid hypoplasia of the bone marrow. In seven patients, a significant increase in erythroid activity occurred, and in four of these, the hemoglobin levels exceeded 16 gm%. It was apparent that a minimum period of at least two months was required to provoke this effect.

Adrenal steroid therapy was administered to some of these patients prior to the use of androgenic hormone. The adrenal steroid alone was ineffective. Whether the adrenal steroid was necessary to evoke the effect in those patients receiving both hormones is not clear, though earlier studies in metastatic breast cancer have suggested that the rate of increase in erythropoiesis and the maximum values attained are greater with combined therapy.²

The improvement in the erythropoietic state of the patients with lymphatic leukemia was associated with increases in WBC counts. That this increase is directly related to the androgenic hormone is not clear, but other observations have suggested that the androgenic hormone may have a stimulating effect on WBC metabolism.⁶ The increase in the WBC count to abnormally high levels required the administration of anti-leukemic chemotherapy in four patients which was effectively carried out. In three patients an increase of the platelet count towards normal was observed. It could not be ascertained whether this was the result of direct stimulation of the platelets or whether the platelet count rose along with the generalized increased cellularity of the stimulated bone marrow. Since the administration of cytotoxic agents was frequently contraindicated in the presence of an initially hypoplastic marrow, the response to the androgenic hormone was a demonstration of the usefulness of this hormone as an adjuvant to cancer chemotherapy.

It would appear that once the erythropoietic response from androgen therapy was obtained, the maintenance of therapy at lower doses or less frequent intervals is necessary. Three patients have now been treated for more than two years. The slow discontinuance of the adrenal steroid therapy may be possible.

In lymphatic leukemia characterized by erythroid hypoplasia of the bone marrow and anemia, the administration of androgenic hormone appears to be indicated and it is effective when employed at a massive dose for a prolonged period.

Summary

Twelve patients with subacute or chronic lymphatic leukemia characterized by erythroid hypoplasia and anemia were treated with massive doses of androgenic hormone. Increases in erythropoiesis to normal or above normal levels of hemoglobin occurred in seven patients. Maintenance therapy is recommended.

The hematological studies were performed by Miss Kay Newton.

The testosterone enanthate was supplied by the Squibb Institute for Medical Research, Brunswick, New Jersey.

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Generic and Trade Names of Drugs

Fluoxymesterone—*Halotestin, Ultandren*.

Testosterone enanthate—*Delatestryl*.

Prednisone—*Deltrasone, Delta, Meticorten, Paracort*.

Chlorambucil—*Leukeran*.

Cyclophosphamide—*Cytoxan*.

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Morning Glory Seed Reaction

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DURING the past 18 months, there have been sporadic references in the literature and in the popular press to the ingestion of the lowly morning glory (*Ipomoea*) seed. This phenomenon is apparently one more evidence of man's search for substances that will profoundly affect his thinking and his feeling.

For centuries mankind has sought new experiences by deliberate ingestion of substances having mind-altering properties. The early discovery of herbs or plants with the ability to alter perceptions or states of consciousness was entirely accidental and the search for such substances purely on a trial and error basis. It was soon learned that vegetable alkaloids contained in plants having such properties were responsible for the production of psychic phenomena. An impressive list of such plants, including cahobe, betel nut, muscari, soma, peyote, and the seed of the morning glory is now available as a result of scientific investigation. One of the earliest results accruing from the use of scientific methodology was the observance in Mexico by Louis Lewin¹ of the effects of ingestion of the peyote plant. The active alkaloid, mescaline, was soon isolated from peyote.

Nearly 50 years after the isolation of mescaline, d-lysergic acid diethylamide (LSD) was discovered. This much more powerful psychotogen is found in ergot and various ergot derivatives. Recently, the ololiuqui seed from Central America and Mexico has received considerable attention although it had been recognized as hallucinogenic by the Indians for centuries. In their culture the seed was utilized in religious ecstasies, as a healing agent, and for initiating temporary psychotic states as we now know them. According to Osmond,² Schultes identified ololiuqui as *Rivea corymbosa* in 1941. Today several species of morning glory readily grow in the US, including *Ipomoea tricolor*. A. Hoffmann, in 1960, was able to isolate, among other compounds,

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d-lysergic acid amide and d-isolysergic acid amide from ololiuqui seeds. According to Cohen and Dittman,³ this was the first isolation of psychotogenic or psychotogenic-like substances from the seed of tropical morning glory.

Psychotomimetics are indoles for the most part, whether occurring in plants or animals or as a result of synthesis. These include LSD, adrenochrome, adrenolutin, harmine, bufotenin, and psilocybin, among others. Those not derived from the indole grouping are mescaline and other substances with structures similar to epinephrine and certain parasympathomimetics of more recent vintage.⁴ The most active of the ergot psychotomimetics is LSD with other related compounds, such as lysergic acid monoethylamide and methyl d-lysergic acid diethylamide being much less potent. It may well be that the hallucinogenic action of the morning glory seed originates in LSD-related compounds but to what extent they are psychotogens remains to be substantiated.

Report of a Case

A 20-year-old white female university student presented at the dispensary at 2:30 PM having ingested five packets (250 seeds) of morning glory seeds (*Ipomoea tricolor*) at 11:45 AM. On examination, she was conscious although moderately dissociated. She was alternately weeping and silly in her response to questioning. Neurological examination revealed flushed facies, dilated fixed pupils equal in size and moderately hyperactive (3+) deep tendon reflexes throughout. Her blood pressure reading was 116/60 mm Hg; pulse rate was 76 beats per minute. Within two hours she complained of feelings of tension and anxiety. She repeatedly expressed a fear of losing her mind. By six hours post-ingestion, the tension had subsided and both the dissociative state and weeping had disappeared. From this point on, she was able to communicate in a normal fashion. She revealed no frank hallucinatory phenomena but reported increased awareness of colors and some memory defect, although the latter was more apparent than real.

From the physical standpoint, there was little of great significance. Her temperature was below normal except for two readings during her four-day hospital stay. Her pulse rate varied from 76 to 40 beats per minute, averaging 55. The blood pressure ranged from 132/60 to 92/32 mm Hg, the diastolic readings fluctuating more than the systolic. There was no nausea or vomiting but she had three explosive diarrheic bowel movements nine hours after ingestion of the seeds. This afforded evident relief of generalized abdominal discomfort. There was frequency of urination during the first 12 hours only. Successive urinalyses in 12 and 24 hours were completely within normal limits as was a complete blood count.

Treatment consisted of bed rest, fluids, and no medication. Tranquilizing agents were considered but during the acute phase we had conflicting reports as to the actual substance ingested and calmative drugs were unnecessary once the acute phase had subsided. Fluids were forced following the acute phase. A repeat neurological examination in 24 hours revealed less active (2+) deep tendon reflexes although the pupils continued to be dilated for 48 hours. The patient was discharged on the fourth day when pulse and blood pressure readings had stabilized at or near her norm as recorded in her health record.

Two follow-up outpatient sessions revealed no neurological abnormalities. Dynamically, a hysteroid personality was revealed with deep, unsatisfied dependent needs. Although insisting she took the morning glory seeds out of sheer boredom, it is notable that this episode rallied divorced parents to her support.