PRODUCT MONOGRAPH

DECADRON

(dexamethasone tablets, MSD Std.)

Corticosteroid

MERCK SHARP & DOHME,
CANADA LIMITED/LIMITEE,
KIRKLAND (MONTREAL) QUEBEC.

DATE OF PREPARATION:
JUNE 20, 1979

1201D

NAME OF DRUG

DECADRON

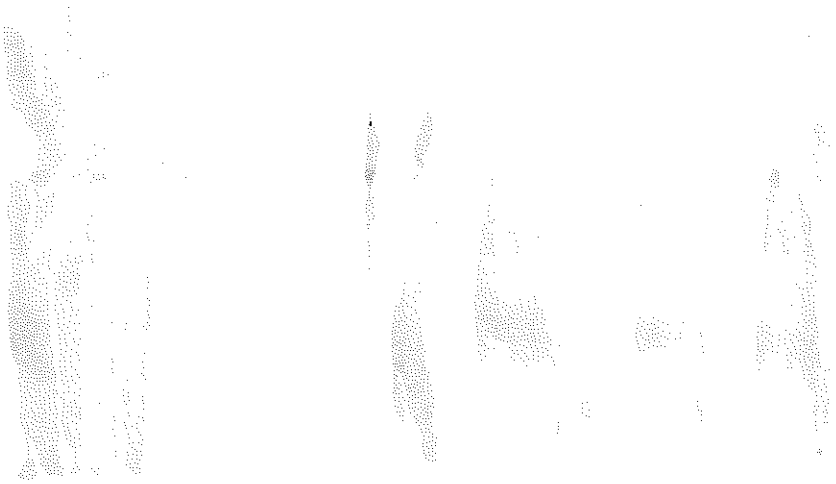
(dexamethasone tablets, MSD Std.)

THERAPEUTIC OR PHARMACOLOGICAL CLASSIFICATION

Corticosteroid

STRUCTURAL FORMULA AND CHEMISTRY

Dexamethasone



Molecular Formula: $C_{22}H_{29}FO_5$ Molecular Weight: 392.47

Chemical Name: 9-fluoro-11β,17,21-trihydroxy-16α-methylpregna-1, 4-diene-3, 20-dione.

Description:

Dexamethasone is a white to practically white, odorless, crystalline powder with a melting point of about 250°C (decomposition). It is very slightly soluble in water (0.1 mg per ml).

ACTION

Dexamethasone possesses the actions and effects of other basic glucocorticoids; it is among the most active members of its class, and is used primarily for its potent anti-inflammatory effects. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. They cause profound and varied metabolic effects and, in addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS

1. Allergic States

Control of severe or incapacitating allergic conditions not responsive to adequate trials of conventional treatment:
Seasonal or perennial allergic rhinitis
Bronchial asthma
Laryngeal edema
Contact dermatitis
Atopic dermatitis
Serum sickness
Drug hypersensitivity reactions

2. Rheumatic Disorders

As adjunctive therapy for short-term administration during an acute episode or exacerbation of:
Psoriatic arthritis
Rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
Ankylosing spondylitis
Acute and subacute bursitis
Acute nonspecific tenosynovitis
Acute gouty arthritis

3. Dermatologic Diseases

Pemphigus
Bullous dermatitis herpetiformis
Severe erythema multiforme (Stevens-Johnson syndrome)
Exfoliative dermatitis
Mycosis fungoides
Severe psoriasis
Severe seborrheic dermatitis.

4. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as -
Allergic conjunctivitis
Keratitis
Allergic corneal marginal ulcers
Herpes zoster ophthalmicus
Iritis and iridocyclitis
Chorioretinitis
Anterior segment inflammation
Diffuse posterior uveitis and choroiditis
Optic neuritis
Sympathetic ophthalmia

5. Endocrine Disorders

Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable, in infancy mineralocorticoid supplementation is of particular importance)
Congenital adrenal hyperplasia
Nonsuppurative thyroiditis
Hypercalcemia associated with cancer

6. Respiratory Disease

Symptomatic sarcoidosis
Loeffler's syndrome not manageable by other means
Berylliosis
Fulminating or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy
Aspiration pneumonitis

7. Hematologic Disorders

Idiopathic thrombocytopenic purpura in adults
Secondary thrombocytopenia in adults
Acquired (autoimmune) hemolytic anemia
Erythroblastopenia (RBC anemia)
Congenital (erythroid) hypoplastic anemia

8. Neoplastic Diseases

For palliative management of:
Leukemias and lymphomas in adults
Acute leukemia of childhood

9. Edematous States

To induce a diuresis or remission of proteinuria in the nephrotic syndrome without uremia, of the idiopathic type or that due to lupus erythematosus.

Cerebral Edema: DECADRON Tablets may be used to treat patients with cerebral edema from various causes. Patients with cerebral edema associated with primary or metastatic brain tumors may benefit from oral administration of DECADRON. It may be used also in the preoperative preparation of patients with increased intracranial pressure secondary to brain tumors, and also for palliation of patients with inoperable or recurrent brain neoplasms, and in the management of cerebral edema associated with neurosurgery. Some patients with cerebral edema due to head injury or pseudotumor cerebri also may benefit from therapy with oral DECADRON. Its use in cerebral edema is not a substitute for careful neurosurgical evaluation and definitive management, such as neurosurgery or other specific therapy.

10. Gastrointestinal Diseases

During a critical period of the disease in:
Ulcerative colitis
Regional enteritis

11. Miscellaneous

Tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate anti-tuberculous chemotherapy.
Trichinosis with neurologic or myocardial involvement.
During an exacerbation or as maintenance therapy in selected cases of -
Systemic lupus erythematosus
Acute rheumatic carditis

12. Diagnostic testing of adrenocortical hyperfunction

CONTRAINDICATIONS

Systemic fungal infections.
Hypersensitivity to this drug.

WARNINGS

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

While on corticosteroid therapy patients should not be vaccinated against smallpox because of potential complications. Conversely, patients with vaccinia should not receive corticosteroid therapy. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high doses, because of possible hazards of neurological complications and a lack of antibody response. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Usage in Pregnancy and Nursing Mothers

Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy or women of child-bearing potential requires that the anticipated benefits be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacologic doses of corticosteroids should be advised not to nurse.

The use of DECADRON Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in

patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. Moreover, corticosteroids may affect the nitrobluetetrazolium test for bacterial infection and produce false negative results. If corticosteroids have to be used in the presence of bacterial infections, appropriate vigorous anti-infectious therapy must be instituted.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

PRECAUTIONS

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

When large doses are given, some authorities advise that corticosteroids be taken with meals and antacids taken between meals to help to prevent peptic ulcer.

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. If the

patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Steroids should be used with caution in: nonspecific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer, renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Fat embolism has been reported as a possible complication of hypercortisonism.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to framk psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Psychological and/or physiological dependency may develop with long-term use, of corticosteroids. Withdrawal symptoms, including anorexia, vague pains, weakness and lethargy may occur.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Phenytoin, phenobarbital, ephedrine and rifampin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring adjustment in corticosteroid dosage. These interactions may interfere with dexamethasone suppression tests which should be interpreted with caution during administration of these drugs.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have

altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalemia.

ADVERSE REACTIONS

Fluid and Electrolyte Disturbances

Sodium retention
Fluid retention
Congestive heart failure in susceptible patients
Potassium loss
Hypokalemic alkalosis
Hypertension

Musculoskeletal

Muscle weakness
Steroid myopathy
Loss of muscle mass
Osteoporosis
Vertebral compression fractures
Aseptic necrosis of femoral and humeral heads
Pathologic fracture of long bones

Gastrointestinal

Peptic ulcer with possible perforation and hemorrhage
Pancreatitis
Abdominal distention
Ulcerative esophagitis

Dermatologic

Impaired wound healing
Thin fragile skin
Petechiae and ecchymoses
Erythema

Dermatologic (cont'd)

Increased sweating
May suppress reactions to skin tests
Other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema.

Neurologic

Convulsions
Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment
Vertigo
Headache

Endocrine

Menstrual irregularities
Development of Cushingoid state
Suppression of growth in children
Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness
Decreased carbohydrate tolerance
Manifestations of latent diabetes mellitus
Increased requirements for insulin or oral hypoglycemic agents in diabetes

Ophthalmic

Posterior subcapsular cataracts
Increased intraocular pressure
Glaucoma
Exophthalmos

Metabolic

Negative nitrogen balance due to protein catabolism

Other

Hypersensitivity
Thromboembolism
Weight gain
Increased appetite
Nausea
Malaise
Psychological and/or physiological dependency

Treatment of accidental ingestion

There is no known antidote but gastric lavage should be performed.

PHARMACOLOGY

DECADRON is a synthetic adrenocortical steroid with the basic actions and effects of other glucocorticoids, but in different degrees. While its anti-inflammatory activity is marked, even with low doses, its effect on electrolyte metabolism is slight. Therefore, electrolyte imbalance is not ordinarily a therapeutic problem with dexamethasone as it has been with some of its predecessors. In low or average doses, dexamethasone usually does not cause elevation of blood pressure, salt and water retention or excessive potassium excretion.

Dexamethasone possesses the actions and effects of other basic glucocorticoids, and is among the most active members of its class. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. They cause profound and varied metabolic effects and, in addition, they modify the body's immune responses to diverse stimuli.

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs including dexamethasone are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Dexamethasone has predominant glucocorticoid activity with little propensity to promote renal retention of sodium and water. Therefore, it does not offer complete replacement therapy, and must be supplemented with salt and/or desoxycorticosterone. Cortisone and hydrocortisone also act predominantly as glucocorticoids, although their mineralocorticoid action is greater than that of dexamethasone. Their use in patients with total adrenocortical insufficiency also may require supplemental salt, or desoxycorticosterone, or both. Fluorocortisone, on the other hand, has the tendency to retain more salt; however, in doses that provide adequate glucocorticoid activity, it may induce edema.

DOSAGE AND ADMINISTRATION

DECADRON Tablets are available in three dose sizes containing 0.5 mg, 0.75 mg and 4.0 mg of dexamethasone respectively.

Administration is governed by the following general principles:

1. Dosage must be individualized according to the severity of the disease and the response of the patient. The severity, prognosis, expected duration of the disease and the reaction of the patient to medication are primary factors in determining dosage. (For infants and children, the recommended doses usually will have to be reduced, but dosage should be dictated by the severity of the condition rather than by age or body weight).

2. Hormone therapy is an adjunct to, not a replacement of conventional therapy, which should be instituted as indicated.

3. Dosage must be decreased or therapy discontinued gradually when administration has been continued for more than a few days.

4. Continued supervision of the patient after cessation of corticosteroids is essential; since there may be a sudden reappearance of severe manifestations of the disease for which the patient was treated.

In acute conditions where prompt relief is urgent, large doses are permissible and may be mandatory for a short period.

In chronic conditions requiring long-term therapy, the lowest dosage that provides adequate, but not necessarily complete, relief should be used. If a high dosage for prolonged periods is considered essential, patients must be observed closely for signs that might necessitate a reduction in dosage or discontinuance of the hormone.

Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be discontinued gradually.

Routine laboratory studies such as urinalysis, two-hour post-prandial blood sugar, determinations of blood pressure and body weight, and a chest X-ray should be carried out at regular

intervals during prolonged therapy. Periodic determinations of serum potassium are advisable if large doses are being used. Upper gastrointestinal X-rays should be taken when treatment is prolonged, in patients with history of ulcer or when there is gastric distress.

Patients may be transferred to DECADRON from any other glucocorticoid with the proper adjustment in dosage.

The following milligram equivalents facilitate changing to DECADRON from other glucocorticoids.

DECADRON	Methylprednisolone and Triamcinolone	Prednisolone and Prednisone	Hydrocortisone	Cortisone
0.75 mg=	4 mg=	5 mg=	20 mg=	25 mg=

Milligram for milligram, dexamethasone is approximately equivalent to betamethasone, four to six times more potent than methylprednisolone and triamcinolone, six to eight times more potent than prednisone and prednisolone, 25 to 30 times more potent than hydrocortisone, and about 35 times more potent than cortisone. At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone and closely related derivatives of hydrocortisone.

Specific Dosage Recommendations

In chronic, usually nonfatal diseases, including endocrine and chronic rheumatic disorders, edematous states, respiratory and gastrointestinal diseases, some dermatologic diseases and hematologic disorders, start with a low dose (0.5 to 1 mg a day) and gradually increase dosage to the smallest amount that gives the desired degree of symptomatic relief.

Dosage may be administered two, three or four times a day.

When symptoms have been suppressed adequately, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects. When the optimal maintenance dosage has been determined, regardless of the initial daily schedule, therapy often is successful on a twice-a-day regimen.

In congenital adrenal hyperplasia, the usual daily dose is 0.5 to 1.5 mg.

In acute, nonfatal diseases, including allergic states, ophthalmic diseases, acute and subacute rheumatic disorders, dosage ranges between 2 and 3 mg a day; however, higher doses are necessary in some patients. Since the course of these conditions is self-limited, prolonged maintenance therapy is not usually necessary.

Dual Therapy

In acute, self-limited allergic disorders or acute exacerbations of chronic allergic disorders (e.g. acute allergic rhinitis, acute attacks of seasonal allergic bronchial asthma, urticaria medicamentosa, angioneurotic edema and contact dermatoses), the following dosage schedule, combining parenteral and oral therapy, is suggested:

First Day:	1 or 2 ml (4 or 8 mg), intramuscularly, of Injection DECADRON Phosphate.
Second Day:	2 Tablets DECADRON (0.75 mg) twice a day.
Third Day:	2 Tablets DECADRON (0.75 mg) twice a day.
Fourth Day:	1 Tablet DECADRON (0.75 mg) twice a day.
Fifth Day:	1 Tablet DECADRON (0.75 mg) per day.
Sixth Day:	1 Tablet DECADRON (0.75 mg) per day.
Seventh Day:	No treatment.
Eighth Day:	Follow-up visit.

In chronic, potentially fatal diseases such as systemic lupus erythematosus, pemphigus, symptomatic sarcoidosis, the recommended initial dosage is 2 to 4.5 mg a day; higher doses are necessary in some patients.

As soon as adequate relief is obtained, the dosage should be reduced gradually to the minimum amount that will produce the desired therapeutic effect.

When the disease is acute and life-threatening (e.g., acute rheumatic carditis, crisis of systemic lupus erythematosus, severe allergic reactions, pemphigus, neoplastic disease), the initial dosage is between 4 and 10 mg a day, administered in at least four divided doses; this dosage may have to be increased in some patients to establish control. As soon as control is attained, the dosage should be reduced gradually to the minimum amount that will maintain relief.

When an extremely rapid onset of action is desired, Injection DECADRON Phosphate may be administered intravenously for the first two or three doses.

Epinephrine is the drug of immediate choice in severe allergic reactions. DECADRON Tablets are useful either concurrently or as supplementary therapy.

In cerebral edema, DECADRON Phosphate Injection is administered initially in acute conditions. When maintenance therapy is required, this should be changed to oral DECADRON as soon as possible. For palliative management of patients with recurrent or inoperable brain tumors, maintenance therapy should be individualized with either DECADRON Phosphate Injection or DECADRON Tablets. A dosage of 2 mg two or three times a day may be effective. The smallest dosage necessary to control cerebral edema should be utilized.

In the adrenogenital syndrome, daily dosages of 0.5 to 1.5 mg may keep children in remission and prevent the recurrence of abnormal excretion of 17-ketosteroids.

As massive therapy in certain conditions, such as acute leukemia, the nephrotic syndrome, and pemphigus, the recommended dosage is from 10 to 15 mg a day. Patients receiving such a high dosage must be observed very closely for the appearance of severe reactions.

Dexamethasone suppression tests

1. Tests for Cushing's syndrome

   Give 1.0 mg of DECADRON orally at 11:00 p.m. Blood is drawn for plasma cortisol determination at 8:00 a.m. the following morning.

For greater accuracy, give 0.5 mg of DECADRON orally every 6 hours for 48 hours. Twenty-four hour urine collections are made for determination of 17-hydroxy-corticosteroid excretion.

2. Test to distinguish Cushing's syndrome due to pituitary ACTH excess from Cushing's syndrome due to other causes. Give 2.0 mg of DECADRON orally every 6 hours for 48 hours. Twenty-four hour urine collections are made for determination of 17-hydroxycorticosteroid excretion.

AVAILABILITY

Tablets DECADRON are compressed, pentagonal-shaped tablets colored to distinguish potency, scored on one side with the MSD code on the other side. They are available as follows:

Ca 7601 - Pale bluish-green tablets, each containing 0.75 mg of dexamethasone, MSD Std., coded MSD 63 supplied in bottles of 100 and 500.

Ca 7598 - Yellow tablets, each containing 0.5 mg of dexamethasone, MSD Std., supplied in bottles of 100.

Ca 7645 - White tablets, each containing 4.0 mg of dexamethasone, MSD Std., coded MSD 97, supplied in bottles of 50.

REFERENCES

A Decade of Anti-Inflammatory Steroids, From Cortisone to Dexamethasone, Ann. New York Acad. Sc. 83:797, October 14, 1959 (entire issue).

Abrahamson, I.A., Jr., and Abrahamson, I.A., Sr.: Dexamethasone - A Preliminary Clinical Study, Ohio M.J. 55:959, July 1959.

Adams, D.A., Maxwell, M.H., and Bernstein, D.: Corticosteroid Therapy of Glomerulonephritis and the Nephrotic Syndrome: A Review, J. Chron. Dis. 15:29, January 1962.

Arth, G.E., et al.: 16-Methylated Steroids. 16α-Methyl Analogs of Cortisone. A New Group of Anti-Inflammatory Steroids. 9α-Halo Derivatives, J. Am. Chem. Soc. 80:3161, June 20, 1958 (Communications to the Editor).

Atkinson, N.N.: Corticosteroid Therapy in Arthritis Patients with Hypertension and/or Cardiac Disorders, J.M. Soc. New Jersey 58:542, November 1961.

Baderman, H., and Maguire, C.: Cataract and Steroids, Brit. M.J. 2:108, July 9, 1961 (in Correspondence).

Bagnall, A.W.: Practical Points in the Present-Day Management of Patients with Rheumatic Disease, Arch. Interam. Rheumat. 2:89, March 1959.

Barnett, S.M.: Dexamethasone in Short-Term Dermatological Conditions, Wisconsin M.J. 58:699, December 1959.

Barros Barreto, H.P., and Recant, L.: Tolbutamide Studies in Prediabetes, Ann. New York Acad. Sc. 82:560, Sept. 25, 1959.

Bendersky, G., et al.: Massive Steroid Therapy in Acute Rheumatic Activity and Carditis, Circulation 22:722, October 1960 (Part 11) (in Soc. Proc.).

Bird, C.E.: Agranulocytosis Due to Imipramine (Tofranil), Canad. M.A.J. 82:1021, May 14, 1960.

Black, R.L., Oglesby, R.B., von Sallmann, L., and Bunim, J.J.: Posterior Subcapsular Cataracts Induced by Corticosteroids in Patients with Rheumatoid Arthritis, J.A.M.A. 174:166, Sept. 10, 1960 (in Preliminary Communication).

Black, R.L., et al.: Dexamethasone: Antirheumatic Properties, Hormonal Effects and Adverse Reactions (A 16 Month Study), Arth. & Rheumat. 3:112, April 1960.

Blinderman, E.: Effect of Dexamethasone on Mitochondria in 'Anoxic Brain' Arch. Neurol. 12:278, March 1965.

Boland, E.W.: 16α-Methyl Corticosteroids - A New Series of Anti-Inflammatory Compounds: Clinical Appraisal of Their Antirheumatic Potencies, California Med. 88:417, June 1958.

Boland, E.W.: Clinical Observations with 16α-Methyl Corticosteroid Compounds. Preliminary Therapeutic Trials with Dexamethasone (16α-Methyl 9α-Fluoroprednisolone) in Patients with Rheumatoid Arthritis, Ann. Rheumat. Dis. 17:376, Dec. 1958.

Boland, E.W., and Headley, N.E.: Preliminary Clinical Observations with a New Series of Synthetic Corticosteroid Compounds in Patients with Rheumatoid Arthritis, Arth. & Rheumat. 2:81, February 1959 (in Soc. Proc.).

Boland, E.W.: Chemically Modified Adrenocortical Steroids. An Appraisal of Their Relative Therapeutic Efficiencies in Rheumatoid Arthritis, J.A.M.A. 174:835, October 15, 1960.

Boland, E.W.: Clinical Comparison of the Newer Anti-Inflammatory Corticosteroids, Ann. Rheumat. Dis. 21:176, June 1962.

Brown, E.A.: The Suppression of the Supervenient Symptoms of Ragweed Pollinosis with Dexamethasone, Antibiotic Med. 6:412, July 1959.

Brown, E.B., Seideman, T., Seigelaub, A.B., and Popovitz, C.: Statistical Study of the Therapeutic Ratio of Dexamethasone (DECADRON), A New Corticosteroid, J. Allergy 30:484, Nov-Dec. 1959.

Bulgrin, J.G., DuBois, E.L., and Jacobson, G.: Peptic Ulcer Associated with Corticosteroid Therapy: Serial Roentgenographic Studies, Radiology 75:712, November 1960.

Bundy, W.E.: A Survey of Steroid Therapy in Children, West Virginia M.J. 57:203, June 1961.

Bunim, J.J., et al.: Studies on Dexamethasone, A New Synthetic Steroid, in Rheumatoid Arthritis-A Preliminary Report. Adrenal Cortical, Metabolic and Early Clinical Effects, Arth. & Rheumat. 1:313, August 1958.

Butterworth, T., and Strean, L.P.: The Synergism of Salicylates and Steroids, Arch. Dermat. 84:964, December 1961.

Byers, R.K., Bergman, A.B., and Joseph, M.C.: Steroid Myopathy, Pediatrics 29:26, January 1962.

Cagli, V., DeNardo, U., and Raymondi, G.: Metabolic Effects and Clinical Results of Dexamethasone in the Treatment of Bronchial Asthma, Minerva med. 50:941, March 31, 1959 (abstr. J.A.M.A. 170:2255, August 29, 1959).

Cataracts Caused by Corticosteroids, Arch. Ophth. 66:455, October 1961 (in Editorials).

Cerutti, P.: Action of 9 Alpha-Fluoro-16 Alpha Methylprednisolone or Dexamethasone in the Treatment of Certain Skin Diseases: Consideration of Various Cortisone Derivatives, Minerva med. 50:917, March 31, 1959 (abstr. J.A.M.A. 171:360, Sept. 19, 1959).

Chears, W.C., Jr., et al.: The Gluten-Free Diet in Nontropical Sprue of Adults, South. M.J. 56:38, January 1963.

Chervinsky, P.: The Use of Dexamethasone in the Treatment of Allergic Disorders, Ann. Allergy 17:714, Sept.-Oct. 1959.

Clinical Experience with Triamcinolone and Dexamethasone, Ann. Rheumat. Dis. 18:59, March 1959 (in Heberden Soc., Reports of Meetings).

Cohen, A., et al.: Treatment of Rheumatoid Arthritis with Dexamethasone. Two Hundred Fifty-One Patients Treated for Short and Long periods, J.A.M.A. 174:831, October 15, 1960.

Cohen, D.D.: Bell's Palsy-A Medical Emergency, J.A.M.A. 173:1563, August 6, 1960.

Conway, H., Gillette, R., Smith, J.W., and Findley, A.: Differential Diagnosis of Keloids and Hypertrophic Scars by Tissue Culture Technique with Notes on Therapy of Keloids by Surgical Excision and DECADRON, Plast. & Reconstruct. Surg. 25:117, February 1960.

Craig, D.M.: The Management of Congestive Heart Failure, J. Lancet 80:20, January 1960.

Dall, J.L.C., and Buchanan, J.: Steroid Therapy in Heart-Block Following Myocardial Infarction, Lancet 2:8, July 7, 1962.

DeCourt, J., Jayle, M.F., Michard, J.P., and Mauvais, P.: Use of Dexamethasone in Adrenal Cortex Inhibition Tests, Semaine Hôp. Paris 36:351, Feb. 4, 1960 (abstr. J.A.M.A. 173:595, June 4, 1960).

Dexamethasone, J.A.M.A. 172:1313, March 19, 1960 (in Foreign Letters, Germany).

Dexamethasone for Asthma, J.A.M.A. 173:834, June 18, 1960 (in foreign Letters, France).

Dexamethasone for Polyarthritis, J.A.M.A. 171:239, Sept. 12, 1959 (in Foreign Letters, Norway).

Dexamethasone for Rheumatic Disease, J.A.M.A. 172:1415, March 26, 1960 (in Foreign Letters, France).

Domonkos, A.N.: Pemphigus Vulgaris, Arch. Dermat. 80:498, Oct. 1959 (in Soc. Transactions).

Dragovich, J.J.: Infectious Asthma, Northwest Med. 60:710, July 1961.

DuBois, E.L. Bulgrin, J.G., and Jacobson, G.: The Corticosteroid-Induced Peptic Ulcer: A Serial Roentgenological Survey of Patients Receiving High Dosages, Am. J. Gastroenterol. 33:435, April 1960.

DuBois, E.L.: Current Therapy of Systemic Lupus Erythematosus. A Comparative Evaluation of Corticosteroids and Their Side Effects with Emphasis on Fifty Patients Treated with Dexamethasone, J.A.M.A. 173:1633, August 13, 1960.

DuBois, E.L., and Adler, D.C.: Single-Daily Dose Oral Administration of Corticosteroids in Rheumatic Disorders: An Analysis of its Advantages, Efficacy, and Side Effects, Curr. Therap. Res. 5:43, Feb. 1963.

Duvenci, J., Chodosh, S., and Segal, M.S.: Dexamethasone Therapy in Bronchial Asthma, Ann. Allergy 17:695, Sept.-Oct. 1959.

Eisert, J., Hannibal, J.E., Jr., and Sanders, S.L.: Fatal Amebiasis Complicating Corticosteroid Management of Pemphigus Vulgaris, New England J. Med. 261:843, October 22, 1959.

Epstein, J.A., and Kupperman, H.S.: Dexamethasone Therapy in the Adrenogenital Syndrome - A Comparative Study, J. Clin. Endocrinol. 19:1503, Nov. 1959 (in Letters to the Editor).

Eskin, B.A., Laufer, E.U., and Pettit, M.D.: Hemolytic Disease of the Newborn Due to the Good Factor, Am. J. Obst. & Gynec. 81:997, May 1961.

Evans, E.G., Jr., McDonald, L.B., and Porter, R.A.: Silo-Filler's Disease. Report of Two Cases in Henderson County, North Carolina, North Carolina, M.J. 21:59, February 1960.

Falliers, C.J., and Bukantz, S.C.: Dexamethasone in Childhood Asthma, Ann. Allergy 17:887, Nov.-Dec. 1959.

Farkas, E.: Corticosteroids for Infections, Lancet 1:280, Feb. 4, 1961 (in Letters to the Editor).

Fein, B.T.: Perforation and Inflammation of Diverticula of the Colon Secondary to Long-Term Adrenocorticosteroid Therapy for Bronchial Asthma and Pulmonary Emphysema, South. M.J. 54:355, April 1961.

Finkel, K.C.: Mortality from Varicella in Children Receiving Adrenocorticosteroids and Adrenocorticotropin, Pediatrics 28:436, September 1961.

Font, J.H.: Otorhinolaryngolocical Considerations on the Temporal Arteritis Syndrome, J.A.M.A. 174:853, Oct. 15, 1960.

Fonzari, M.: Notes on the Therapeutics of Pemphigus Foliaceus, Hospital 57:275, Feb. 1960 (abstr. J.A.M.A. 173:850, June 18, 1960).

Ford, H.C., Sellers, A.M., and Weiss, M.M.: Comparison of Cortisone and Dexamethasone as Adrenal Replacement Therapy, Clin. Res. 9:71, Jan. 1961 (in Soc. Proc.).

Freedland, M.E.: Temporal Arteritis. A Report of Two Cases Without Systemic Symptoms, California Med. 92:41, Jan. 1960 (in Case Reports).

French, L.A., and Galicich, J.H.: The Use of Steroids for Control of Cerebral Edema, Clin. Neurosurgery 10:212, 1964.

Friedlaender, A.S., and Friedlaender, S.: Dexamethasone: A New Corticosteroid-Its Effect in Allergic Disease, Ann. Allergy 17:705, Sept.-Oct. 1959.

Friedman, H.T., and Murray, J.F.: Rate of Recovery of Normal Adrenal Cortical Function After Dexamethasone Therapy, J. Allergy 30:272, May-June 1959 (in Soc. Proc.).

Galicich, J.H., and French, L.A.: Use of Dexamethasone in the Treatment of Cerebral Edema Resulting from Brain Tumors and Brain Surgery, Am. Pract. & Digest. Treat. 12:169, March 1961.

Galli, T., and Mannetti, C.: First Orientations on the Therapeutic Possibilities of Dexamethasone in Rheumatology, Minerva med. 50:949, March 31, 1959 (abstr. J.A.M.A. 170:2254, Aug. 29, 1959).

Glass, G.B., Niebergs, H.E., Hitzelberger, A.L., and Telater, H.: Effect of Corticosteroids on Gastric Cytology and Histology in Humans, Clin. Res. 8:200, April 1960 (in Soc. Proc.).

Gold, E.M.: Plasma Clearance and Glucuronide Conjugation of 11-Desoxycortisol (Substance S) in Man, Proc. Soc. Exper. Biol. & Med. 103:829, April 1960.

Golding, D.N., and Begg, T.B.: Dexamethasone Myopathy, Brit. M.J. 2:1129, Oct. 15, 1960.

Goldman, L., and Preston, R.H.: Corticosteroid Therapy of the Common Chronic Eczematous Hand Dermatitis, GP 20:85, Sept. 1959.

Gordon, D.M.: Adrenocortical Steroid Therapy in Ophthalmology, North Carolina M.J. 19:473, November 1958.

Gordon, D.M.: Experiences with Corticosteroids in Ophthalmology, New York J. Med. 59:1041, March 15, 1959.

Gordon, D.M.: The Treatment of Chronic Uveitis. Preliminary Comments on Chronic Degenerative Diseases, Arch. Ophth. 62:400, September 1959.

Gordon, D.M.: Dexamethasone in Ophthalmology, Am. J. Ophth. 48:656, November 1959.

Gordon, D.M.: Use of Dexamethasone in Eye Disease, J.A.M.A. 172:311, January 23, 1960.

Gordon, D.M.: Modern Therapy of Uveitis, Am. J. Ophth. 50:236, August 1960.

Gordon, D.M., Kammerer, W.H., and Freyberg, R.H.: Examination for Posterior Subcapsular Cataracts, J.A.M.A. 175:127, Jan. 14, 1961.

Green, A.: The Newer Steroids, Brit. M.J. 1:647, March 7, 1959 (in Correspondence).

Green, M.A.: Dexamethasone as a Symptomatic Aid in Hay Fever, Ann. Allergy 17:717, Sept.-Oct. 1959.

Hargrove, M.D., Jr., Verner, J.B., Jr., Partick, R.L., and Ruffin, J.M.: Intestinal Lipodystrophy Without Diarrhea. Report of a Case Diagnosed by Intestinal Tube Biopsy, J.A.M.A. 173:1125, July 9, 1960 (in Clinical Notes).

Harley, R.D., and Mishler, J.E.: Dexamethasone in Ophthalmology, J.M. Soc. New Jersey 57:173, April 1960.

Harris, L.C., and Keet, M.P.: Xeroderma Pigmentosum, J. Pediat. 57:759, November 1960.

Harris, R.H., and Taylor, F., Jr.: Pemphigus Vulgaris and Diabetes Mellitus. A Case Report, Arch. Dermat. 80:442, Oct. 1959.

Hart, F.D.: Dexamethasone, Lancet 1:366, Feb. 14, 1959 (in Letters to the Editor).

Hart, F.D., Casey, T.A., and O'Riordan, M.D.: Cataract and Steroids, Brit. M.J. 1:1680, June 10, 1961 (in Correspondence).

Hart, F.D., Golding, J.R., and Brown, G.: Dexamethasone, Lancet 2:255, September 5, 1959.

Hauser, E.: Ménière's Disease: A New Therapeutic Approach, J. Am. Geriatrics Soc. 7:874, November 1959.

Hayles, A.B., et al.: Hirsutism in Adolescent Girls. Possible Stein-Leventhal Syndrome, Am. J. Dis. Child. 100:31, July 1960.

Hitzelberger, A.L., and Glass, G.B.J.: Effect of Corticosteroids on Non-Dialyzable Substances of the Gastric Juice, Fed. Proc. 19:190, March 1960 (Part 1).

Hitzelberger, A.L., and Glass, G.B.: Effects of Corticosteroids in Human Beings on the Secretion of Large Molecular Substances of Gastric Juice, J. Lab. & Clin. Med. 59:575, April 1962.

Hoagland, R.J., Bartelloni, P., and Cataldo, J.R.: Meningococcemia: A Cause of Prolonged Fever, U.S. Armed Forces M.J. 11:1190, October 1960 (in Case Reports).

Hollander, J.L.: Clinical Use of Dexamethasone Role in Treatment of Patients with Arthritis, J.A.M.A. 172:306, Jan. 23, 1960.

Houli, J.: Arch. Interam. Rheumat. 2:167, March 1959 (Questionnaire).

Huschke, V., Haggermüller, F.: Corticoid Therapy of Bulbar and Encephalitic Forms of Poliomyelitis, German M. Monthly 7:342, October 1962.

Incaprera, F.P.: Pulmonary Eosinophilia, Am. Rev. Respir. Dis. 84:730, Nov. 1961 (Part 1) (in Case Reports).

Jalil, M.J., Guerrero, A.R., and Harnccker, J.H.: Evaluation of Methylprednisolone, Triamcinolone, and Dexamethasone in the Treatment of Disseminated Lupus Erythematosus, Rev. med. Chile 88:12, 1960 (abstr. Ann. Rheumat. Dis. 19:392, Dec. 1960).

Josselson, A.J., Hauck, D., and Pote, W.W.H., Jr.: Observations on the Effects of Dexamethasone in Patients with Diabetes Mellitus and Retinitis Proliferans, Clin. Res. 8:109, Jan. 1960 (in Soc. Proc.).

Kalz, F., and Fekete, Z.: Simultaneous Evolution of a Subacute Lupus Erythematosus and of Psoriasis, Arch. Dermat. 80:584, November 1959.

Kanof, N.B., and Blau, S.: Dexamethasone in Dermatology, Arch. Dermat. 80:197, August 1959.

Kelly, H.G., and Hinton, N.A.: The Effect of Dexamethasone and Nitrogen Mustard on the Production of Rheumatoid Factor in Rheumatoid Arthritis, Canad. M.A.J. 88:261, February 2, 1963 (in Soc. Proc.).

Kendall, J.W., and Liddle, G.W.: Virilizing Tumors, South. M.J. 53:289, March 1960 (in Endocrine Clinic).

Klien, B.A.: Nodular Nonsuppurative Panniculitis (Weber-Christian Syndrome) with Relapsing Uveitis, Am. J. Ophth. 48:730, December 1959.

Kohn, C.M., and Grater, W.C.: Dexamethasone in Allergy, Ann. Allergy 17:385, May-June 1959.

Lang, E.F., Jr.: Neurosurgical Management of Intracranial Metastatic Malignancy, S. Clin. North America 47:737, June 1967.

Lichtwitz, A., Hioco, D., and Greslé, C.: One Hundred Patients Treated with Dexamethasone: Comparison with Prednisone and 6-Methylprednisolone, Semaine hôp. Paris 35:1570, May 4, 1959 (abstr. J.A.M.A. 171:483, September 26, 1959).

Lichtwitz, A., Hioco, D., and Greslé, C.: Intolerance, Incidents and Accidents Provoked by Dexamethasone (16 MFP), ibid., p. 1581 (abstr. J.A.M.A. 171:484, September 26, 1959).

Liddle, G.W.: Tests of Pituitary-Adrenal Suppressibility in the Diagnosis of Cushing's Syndrome, J. Clin. Endocrinol. 20:1539, December 1960.

Long, D.M., Hartmann, J.F., and French, L.A.: The Response of Human Cerebral Edema to Glucosteroid Administration. An Electron Microscopic Study, Neurology 16:521, May 1966.

Lymburner, R.M., and Malcolmson, C.H.: Thrombocytopenic Purpura Complicating Infectious Mononucleosis, Canad. M.A.J. 83:652, September 17, 1960 (in Case Reports).

Magnuson, R.H.: Dexamethasone in Chorioretinitis. An Unusaul Case History, Ohio M.J. 57:42, 1961.

Matson, D.D.: Treatment of Cerebral Swelling, New England J. Med. 272:626, March 25, 1965, (in Medical Intelligence).

Moloney, W.C., Davis, S., and Hieber, R.D.: The Use of Steroid Hormones in the Management of Hematologic Disorders, GP 24:100, July 1961.

Moreno, A.R.: Treatment of Gouty Attacks with Steroids, Arch. Interam. Rheumatol. 3:544, December 1960.

Neustadt, D.H.: Corticosteroid Therapy in Rheumatoid Arthritis. Comparative Study of Effects of Prednisone and Prednisolone, Methylprednisolone, Triamcinolone, and Dexamethasone, J.A.M.A. 170:1253, July 11, 1959.

Newman, S., Dorosin, D., and DiRaimondo, V.: Evaluation of the Metabolic Effects of Dexamethasone, Clin. Res. 7:112, Jan. 1959, (in Soc. Proc.).

Nielsen, R.H.: The Use of Dexamethasone in Ophthalmologic Steroid Therapy, Arch. Ophth. 62:438, September 1959.

Oglesby, R.B., Black, R.L., von Sallmann, L., and Bunim, J.J.: Cataracts in Patients with Rheumatic Diseases Treated with Corticosteroids, Arch. Ophth. 66:625, November 1961.

Oski, F.A., Salitsky, S., and Barness, L.A.: Steroid Therapy in Bronchiolitis: A Double-Blind Study, Am. J. Dis. Child. 102:759, November 1961 (in Soc. Proc.).

Parish, F.A.: Treatment of Severe Allergies with Dexamethasone, Ann. Allergy 17:701, Sept.-Oct. 1959.

Paul, W.D.: Systemic Manifestations of Rheumatoid Arthritis (Rheumatoid Disease) Accentuated by Steroid Therapy, J. Iowa M. Soc. 51:205, April 1961.

Perkoff, G.T., et al.: A Delayed Effect of Adrenocortical Steroids on Blood Glucose Levels and Disappearance Rates, Clin. Res. 8:143, Jan. 1960 (in Soc. Proc.).

Pfahl, S.B., Jr., Makley, T.A., Rothermich, N.O., and McCoy, F.W.: The Relationship of Steroid Therapy and Cataracts in Patients with Rheumatoid Arthritis, Am. J. Ophth. 52:831, Nov. 1961 (Part 11).

Popkin, R.J.: Medical Treatment of Peripheral Vascular Diseases, Angiology 12:427, September 1961.

Ramos, J., et al.: Treatment of Lymphoma with High Doses of Dexamethasone Rev. paulista med. 58:1, Jan. 1961 (abstr. J.A.M.A. 176:211, April 15, 1961).

Ramos, J., Jr., Parisi, E., and Mendez, A.G.: Electrocardiographic Alterations During Treatment of Malignant Tumors with Corticoids, Rev. paulista med. 57: Nov. 1960 (abstr. J.A.M.A. 175:183, Jan. 28, 1961).

Rees, R.B., Bennett, J.H., and Greenlee, M.R.: Newer Drug Treatment in Dermatology, California Med. 91:1, July 1959.

Robecchi, A., et al.: On A New Synthetic Cortisonic Substance, Dexamethasone (16-Alpha-Methyl-9-Alpha-Fluoroprednisolone), in the Treatment of Rheumatoid Arthritis, Minerva med. 49:4163, Nov. 10, 1958 (abstr. J.A.M.A. 169:1388 March 21, 1959).

Roberts, H.J.: Treatment of Cerebral Vascular Accidents, J.A.M.A. 173:1507, July 30, 1960 (in Correspondence).

Robinson, H.M., Jr., and Yaffe, S.N.: Follicular Lymphoma, Arch. Dermat. 83:687, April 1961 (in Soc. Proc.).

Rondelet, J.: Preliminary Results in the Clinical Investigation of a New Corticosteroid: Dexamethasone Acetate, Sem. hôp. Paris 35:1526, 1959 (abstr. J. Am. Geriatrics Soc. 8:74, January 1960).

Rothermich, N.O.: Clinical Experiences with Dexamethasone, Ohio M.J. 57:787, July 1961.

Rowe, A.H., and Rowe, A.H., Jr.: Bronchial Asthma - Its Treatment and Control, J.A.M.A. 172:1734, April 16, 1960.

Rubens-Duval, A., Villiaumey, J., and Lubetzki, D.: Results of Treatment with Hexadecadrol in Rheumatology, Semaine hôp. Paris 35:2441, 1959 (abstr. Ann. Rheumat. Dis. 19:195, June 1960).

Rudolph, J.A., and Dudolph, B.M.: Treatment of Dermatologic and Respiratory Allergy with Dexamethasone, Ann. Allergy 17:710, Sept.-Oct. 1959.

Segal, M.S.: Current Status of Therapy in Bronchial Asthma, J.A.M.A. 169:1063, March 7, 1959 (in Council on Drugs).

Silberman, I.A., and Adams, D.A.: The Nephrotic Syndrome and Pregnancy, New England J. Med. 267:1286, Dec. 20, 1962.

Slater, J.D.H., Heffron, P.F., Vernet, A., and Nabarro, J.D.N.: Clinical and Metabolic Effects of Dexamethasone, Lancet 1:173, January 24, 1959.

Sperber, P.A.: Dexamethasone in Dermatologic Therapy, Ann. Allergy 17:895, Nov.-Dec. 1959.

Spies, T.D., Stone, R.E., and Niedermeier, W.: A Note on the Therapeutic Efficacy of 16-Alpha-Methyl-9-Alpha-Fluoroprednisolone (DECADRON), South. M.J. 51:1066, Aug. 1958.

Steroids For Lipoid Nephrosis, J.A.M.A. 173:834, June 18, 1960 (in Foreign Letters, France).

Stoll, B.A.: Dexamethasone in Advanced Breast Cancer, Cancer 13:1074, Sept.-Oct. 1960.

Stresemann, E.: The Dosage of Dexamethasone and Triamcinolone in Bronchial Asthma, Lancet 2:257, Sept. 5, 1959.

Taylor, J.M., Levy, W.A., Herzog, I., and Scheinberg, L.C.: Prevention of Experimental Cerebral Edema by Corticosteroids, Neurology 15:667, July, 1965.

Toogood, J.H., Dyson, C., Thompson, C.A., and Mularchyk, E.J.: Posterior Subcapsular Cataracts as a Complication of Adrenocortical Steroid Therapy, Canad. M.A.J. 86:52, Jan. 13, 1962.

Tow, A.: Steroid Therapy in Dermatitis Venenata (with Case Reports), West Virginia M.J. 56:199, June 1960.

Vickers, M.A.: Brief Oral Therapy of Severe Allergic Dermatoses with Dexamethasone, J. Maine M.A. 51:458, Dec. 1960.

Villa, L., Ballabio, C.B., and Sala, G.: Clinical and Metabolic Effects of 16-Alpha-Methyl-9-Alpha-Fluoroprednisolone ("Dexamethasone"), Reumatismo. 10:127, 1958 (abstr. Ann. Rheumat. Dis. 18:170, June 1959).

Walker, A.E., Stewart, J.J., and Crone, P.J.: Letterer-Siwe Disease (Acute Disseminated Histiocytosis X), Arch. Dermat. 83:159, Jan. 1961 (in Soc. Proc.).

Walton, C.H.A.: Clinical Experience with Dexamethasone, Canad. M.A.J. 81:724, November 1, 1959.

West, H.F.: Corticosteroid Bruising, Ann. Rheumat. Dis. 20:86, March 1961.

West, K.M., et al.: The Physiologic Effects of Dexamethasone, Arth. & Rheumat. 3:129, April 1960.

Wiggins, R.A., Jr., and Canada, R.O., Jr.: A Clinical Note on the Use of Dexamethasone in the Study of Patients Suspected of Hypopituitarism, Military Med. 126:131, Feb. 1961.

Williams, G.T.: A Comparative Evaluation of Newer Corticosteroids in the Treatment of Rheumatoid Arthritis, South. M.J. 52:267, March 1959.

Winkelmann, R.K., Scheen, S.R., Jr., and Underdahl, L.O.: Acanthosis Nigricans and Endocrine Disease, J.A.M.A. 174:1145, Oct. 29, 1960.

Zangara, A., Siccardi, A., and Piccioni, A.: Effect of Prednisone and Dexamethasone on Capillary Permeability in Rheumatic Fever, Reumatismo 11, 191, 1959 (abstr. Ann. Rheumat. Dis. 19:70, March 1960).

Zuckner, J., Ramsey, R.H., and Budd, J.J., Jr., Dexamethasone Therapy with Gastric Function Studies in Patients with Rheumatoid Arthritis, Am. J.M. Sc. 240:58, July 1960.