Aldactazide®
(spironolactone 25 mg./
hydrochlorothiazide 25 mg.)

WARNING

Spironolactone, an ingredient of Aldactazide, has been shown to be a tumorigen in chronic toxicity studies in rats (see *Warnings*). Aldactazide should be used only in those conditions described under *Indications*. Unnecessary use of this drug should be avoided.

Fixed-dose combination drugs are not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: Cirrhosis of the liver accompanied by edema and/or ascites. Essential hypertension, edema of congestive heart failure and the nephrotic syndrome, when other measures are considered inappropriate.

Contraindications: Anuria, acute renal insufficiency, significant impairment of renal function, hyperkalemia or acute or severe hepatic failure. Allergy to thiazide diuretics or to other sulfonamide-derived drugs.

Warnings: Excessive potassium intake may cause hyperkalemia. Potassium supplements should not be given with Aldactazide. Do not administer concurrently with other potassium-sparing diuretics. Sulfonamide derivatives including thiazides have been reported to exacerbate or activate systemic lupus erythematosus.

Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats. In one study using 25, 75 and 250 times the usual daily human dose (2 mg./kg.) there was a statistically significant dose-related increase in benign adenomas of the thyroid and testes. In female rats there was a statistically significant increase in malignant mammary tumors at the mid-dose only. In male rats there was a dose-related increase in proliferative changes in the liver. At the highest dosage level (500 mg./kg.) the range of effects included hepatocytomegaly, hyperplastic nodules and hepatocellular carcinoma; the last was not statistically significant.

Precautions: Patients should be carefully evaluated for possible disturbances of fluid and electrolyte balance. Hyperkalemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Hypokalemia may develop as a result of profound diuresis, particularly when Aldactazide is used concomitantly with loop diuretics, glucocorticoids or ACTH. Transient elevation of BUN may occur. Dilutional hyponatremia or rarely low-salt syndrome may develop. Gynecomastia may develop and in rare instances some breast enlargement may persist.

Thiazides may alter the metabolism of uric acid and carbohydrates with possible hyperuricemia, gout and decreased glucose tolerance. Vascular responsiveness to norepinephrine is reduced. Thiazides may also increase the responsiveness to tubocurarine. Thiazides may decrease serum PBI levels and prolonged therapy may induce hypercalcemia and hypophosphatemia.

Spironolactone may and hydrochlorothiazide does cross the placental barrier. Use in pregnant women requires that the anticipated benefit be weighed against possible hazards to the fetus. Breast feeding should be discontinued when Aldactazide is being used.

Adverse Reactions:

Associated with spironolactone: Gynecomastia is observed not infrequently. Gastrointestinal symptoms including cramping and diarrhea, drowsiness, lethargy, headache, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, inability to achieve or maintain erection, irregular menses or amenorrhea, postmenopausal bleeding, hirsutism and deepening of the voice. Carcinoma of the breast has been reported but a cause-and-effect relationship has not been established.

Associated with thiazides: Gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea, abdominal cramps), purpura, thrombocytopenia, leukopenia, agranulocytosis, dermatologic symptoms (cutaneous eruptions, pruritus, erythema multiforme), paresthesia, acute pancreatitis, jaundice, dizziness, vertigo, headache, xanthopsia, photosensitivity, necrotizing angiitis, aplastic anemia, orthostatic hypotension, muscle spasm, weakness and restlessness.

Adverse reactions are usually reversible upon discontinuation of Aldactazide.

Dosage and Administration

Edema in adults: The usual maintenance dose is one tablet four times daily but may range from one to eight tablets daily depending on the response to the initial titration.

Edema in children: The usual daily maintenance dose should be that which provides 0.75 to 1.5 mg. of spironolactone per pound of body weight (1.65 to 3.3 mg./kg.).

Essential hypertension: Usually two to four tablets daily depending on results of the titration of the individual ingredients.

SEARLE Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Communications Department
Box 5110, Chicago, Illinois 60680

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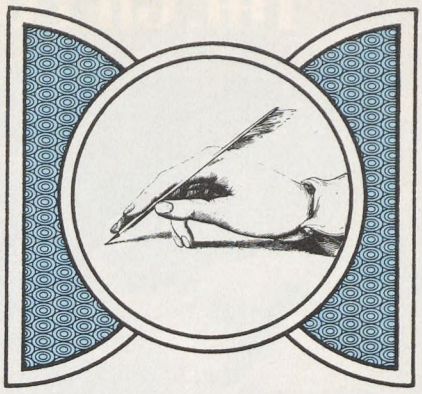
Letters to the Editor



The Journal welcomes Letters to the Editor; if found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with journal style.

Medical School Admissions

To the Editor:

Regarding the October 1976 issue of *The Journal of Family Practice*, I would like to make a comment on Dr. Gayle Stephens' article on reform (*Stephens GG: Reform in the United States: Its impact on medicine and education for family practice. J Fam Pract 3:507-512, 1976).* Dr. Stephens, with his usual perspicacity, has zeroed in on the crux of medical problems, past, present, and future. His article is quite philosophical and his bibliography includes philosophic writers not frequently quoted by current medical writers.

There is one omission in Dr. Stephen's treatise that needs to be pursued if indeed we are to produce, in the future, family physicians with Dr. Stephens' depth of understanding.

Unless there has been a recent change in admission procedures and qualifications, men of his stature and insight are being screened out by admissions committees in favor of the unicentric, single-minded, professional science student whose undergraduate curriculum necessarily restricts study of the broad, historic, political, and philosophic concepts that are so evident in Dr. Stephens' article. Certainly inclusion of philosophy, creative writing, and history should be allowed, if not required.

If, indeed, reform is underway it should include the admission committee concepts of requirements for admission to medical school.

Stephen C. May, MD
Kennesaw, Georgia

Thyroid Disease in Family Practice

To the Editor:

The article entitled "A Study of Thyroid Disease in Family Practice," by J. C. Shank, MD *(J Fam Pract 3:247-252, 1976),* distresses me somewhat. For all its many references and apparent scientific basis, it is in distinct contrast to our teaching and experience at the University of California, Irvine.

It is our impression that hyperthyroidism is a more common condition than myxedema (aside from surgically produced hypothyroidism). We would further hold that a true myxedemic is almost never grossly obese.

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