

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 angitis, 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.

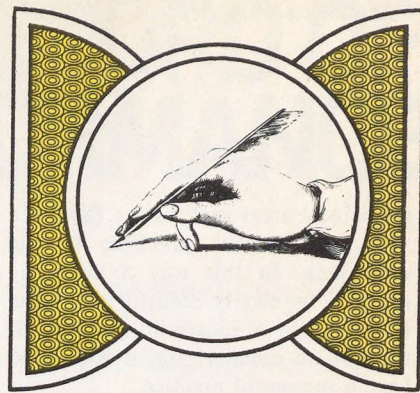
Edema in children: The usual daily maintenance dose should be that which provides 0.75 to 1.5 mg. of spironolactone per pound of body weight (1.65 to 3.3 mg./kg.).

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

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Letters to the Editor



On Obstetrics in Family Practice

To the Editor:

I am writing to respond to Dr. Klein's comments on our paper in a recent edition of the *Journal (J Fam Pract 4:185, 1977)*.

During the training time of the individuals in the practice we studied (Mehl LE, Bruce C, Renner JH: *Importance of obstetrics in a comprehensive family practice. J Fam Pract 3:385, 1976*), there were no family practice residencies. Their background was a rotating internship. Since most family physicians practicing today have this kind of background (although this is changing), it would seem that this is a reasonable way to study practice characteristics. A common way to think about the content of family practice residencies is to study actual practices (whether or not the physicians graduated from a family practice residency). I would agree with Dr. Klein that it would be very interesting to contrast practices composed of individuals having had family practice residencies with individuals trained in rotating internships. Obviously age would have to be controlled for. This is a separate issue, it would seem to me, and not having done this does not prevent us from considering the implications of the data.

Dr. Klein interprets our Table 1 as indicating that those physicians who were secure in their full role of family physicians were happy, while those who were not secure were un-

happy. This seems a reasonable interpretation — although one among several. Because all of the physicians began their practices with similar ideas and enthusiasm (although this is based on their recollections of themselves and on superficial questions, at that — not a thorough personality assessment), it would seem that things changed for them during their practice. The unsatisfied physicians indicated that what bothered them, among other things, was that they were not seeing families and not providing continuous care, but episodic.

The backgrounds of these physicians were grossly similar. The sample sizes were large enough to use the chi-square technique. The differences between the groups may have related to subtle attitudinal differences.

If the family physician cannot compete in a "buyer's marketplace" such as the San Francisco Bay Area, then perhaps there is no need for family practice. We should just train more primary care obstetricians, pediatricians, and internists. Presumably, family practice offers something health-care consumers want. If this is not the case, then perhaps we need to modify our ideas of primary care and family practice. It would seem to me that one of the most interesting ways to understand family practice is to compare successful practices in over-doctored, over-

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