JPP Tweetorial for December 2019

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Day 1 of new series: 7 days of [#spironolactone](https://twitter.com/search?q=%23spironolactone). In the early 1950’s, after aldosterone was extracted and purified, there followed investigation re action & development of antagonists. An oral agent [#spironolactone](https://twitter.com/search?q=%23spironolactone) was approved by the FDA in 1960 & in the UK, early 60s.

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It took until 1987 to clone the mineralocorticoid receptor (MR), via which aldosterone/spironolactone act. By this time, the dose-dependent limitations for use in oedema were known, as poor MR selectivity leads to many sexual ADRs, e.g voice pitch change, breast pain & gynaecomastia.

Day 2: Indications #spironolactone include moderate-severe heart failure (main UK use), oedema associated with ascites, nephrotic syndrome, CHF. Unlicensed uses include resistant hypertension (adjunct).Antiandrogen properties make suitable for acne and hirsutism.

#spironolactone use was revived after the RALES study (1999) showed 30% reduction in heart failure all-cause mortality & #spironolactone is now key to heart failure management pathway.

Day 3: MOA: #spironolactone blocks the mineralocorticoid receptor (MR) inhibiting actions of aldosterone; BP & oedema are reduced & potassium is ‘spared’ in the tubule. The MR receptor is expressed in multiple tissues & adaptive changes in myocardium re heart failure partly driven by aldosterone; blocking activity reduces fibrosis, hypertrophy & inflammation therefore cardio-protective effects

Day 4: Key kinetics: #spironolactone has good oral absorption. It is a prodrug with several active metabolites, released by liver metabolism. Also undergoes enterohepatic recycling. The metabolite canrenone has the longest half-life @15-17hrs. Metabolites excreted urine & faeces.

Dose range 25-50mg heart failure; 25-200mg for oedema associated with liver, kidney, heart disease.

Day 5: Hyperkalaemia (routine monitoring important & care with anything affecting K+ levels, including food), GI disturbance, ataxia, gynaecomastia, menstrual disturbance, leg cramps. Serious; AKI, agranulocytosis, DRESS, SJS.

Sexual ADRs mostly reversible on stopping spironolactone. Eplenerone is an alternative, as more selective to the mineralocorticoid receptor.

Day 6: Caution with any drug increasing K+ levels, e.g ACE inhibitors, ARBs, aliskiren, ciclosporin. Care with NSAIDs re renal impairment & increased K+. #spironolactone can increase lithium & digoxin levels & affect INR. Corticosteroids can oppose K+ sparing effects (not exhaustive).

Day 7: #spironolactone resembles progesterone & can act as an agonist at the progesterone receptor. The testosterone-suppressing effects have led to a role in gender transition (male to female), e.g 100-400mg/day can be used in combination with other drugs (unlicensed use).