Research Update

Spironolactone saves lives in heart failure

The aldosterone antagonist spironolactone cuts the risk of death and the rate of hospitalization by one-third in patients with severe heart failure, according to a large international study. The multicentre study was stopped earlier than planned and its results have been released on the Internet (www.nejm.org) before print publication in the *New England Journal of Medicine*.

The Randomized Aldactone Evaluation Study was conducted in 15 countries on 5 continents, with 1663 patients enrolled in 195 centres. Patients had a ventricular ejection fraction of 35% or less and were receiving standard therapy for heart failure — an angiotensin-converting-enzyme (ACE) inhibitor, a loop diuretic and, in some cases, digoxin. Spironolactone or placebo were added to the regimen on a randomized basis. After follow-up lasting an average of 2 years, the mortality rate was 35% in the spironolactone group and 46% in the placebo group. Spironolactone treatment also lowered the rate of hospitalization and resulted in significant improvement in the symptoms of heart failure. The main side effect is gynecomastia and breast pain, which affected 10% of men taking the drug.

Spironolactone reduces levels of aldosterone, a steroid produced at up to 20 times the normal levels in patients with heart failure. Aldosterone contributes to the sodium retention and edema that characterize the condition. According to an accompanying editorial, "the importance of aldosterone in congestive heart failure has been overlooked in recent years" because ACE inhibitors were thought to eliminate aldosterone production. However, it now appears that ACE inhibitors suppress aldosterone only briefly.

Based on these results, the authors and editorialist recommend adding spironolactone to standard therapy for patients with severe heart failure. — *C.J. Brown*, CMAJ

A new weapon against androgen-independent prostate cancer

A discovery by a scientist at the BC Cancer Agency explains why some prostate cancer tumours grow even without androgen, foiling chemical attempts to stop them. The discovery opens up possibilities for drug therapy to fight these hard-to-control tumours.

The research, by Dr. Marianne Sadar (*J Biol Chem* 1999;274[12]:7777-83), focused on hormone-resistant, or androgen-independent, prostate tumours. The usual treatment for metastasizing prostate cancer is withdrawal of testosterone (androgen), also known as "chemical castration." However, some cancerous prostate cells begin to grow again even without circulating testosterone. How this happens has puzzled scientists for decades. Researchers have known for some time that the growth-promoting effect of testosterone on prostate cancer cells is mediated by the androgen receptor — a protein that is switched on when it binds to testosterone. Sadar discovered that this receptor can be activated without testosterone, a process that may underlie androgen-independent tumour growth. This is occurring in a new region of the receptor, she says, by a mechanism that "we are still figuring out." She and her colleagues are now mapping the androgen receptor sites to find where the receptors are being activated. This is a first step in designing drugs to act as decoys for the receptor. Any new drug would be used in combination with conventional hormone withdrawal therapy. "When the patient is on androgen withdrawal therapy, we should be able to control the cell so that we can control androgen-independent disease," says Sadar.

Dr. Nicholas Bruchovsky, head of the BC Cancer Agency's Department of Cancer Endocrinology, says that "the loss of response to treatment is one of the major stumbling blocks that limits the effectiveness of today's therapies. Dr Sadar's discovery has opened up a whole new approach to possible cures." — © *Heather Kent*, Vancouver

Sale of anonymous prescription data breaches confidentiality: UK court

A recent decision by the United Kingdom's High Court has called into question the assumption that the use of facts and figures gleaned from a physician's prescription data does not constitute a breach in confidentiality. The May 1999 court case in London is thought to be the first to deal with patient information that has been rendered anonymous. Mr. Justice Latham ruled that patients' implied consent covered use of their data for treatment and related purposes only, not for sale to pharmaceutical companies. The case arose after Source Informatics, a US-based company that operates a prescriber database for pharmaceutical companies, sought to approach GPs with promotions and information about their products. The GPs had refused to allow their prescription details to be supplied to the database. Source Informatics was given permission to appeal the judgement because the ruling "raises issues of huge importance for the law of confidentiality."