CANCER REHABILITATION

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Benefits of exercise in cancer prevention and rehabilitation

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Exercise and cancer prevention

- Numerous studies show reduced prevalence in exercisers;
- Being sedentary and overweight could account for 14% (men) and 20% (women) cancer deaths per year;
- 40-50% reduction in bowel cancer in high physical exercisers;
- 15% of colon cancers could have been prevented by 30 minutes of daily exercise (Harvard Centre for Cancer Control)

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The immune system

- 2 immune systems:
- Innate:
  - 1st line of defence
  - Includes skin, mucous, defence enzymes, immunoglobulin, organ lining and endothelial cells, chemical and biological agents (NK cells, macrophages, neutrophils.

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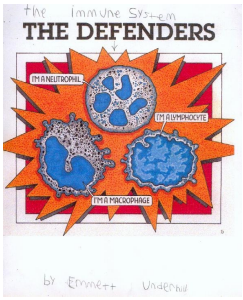
The innate system

- Immediate defence;
- Non-antigen specific;
- No antigen memory.



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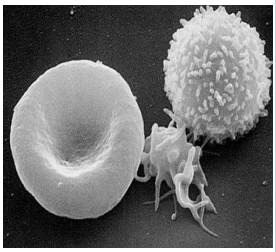
The adaptive system

- Consists of B-cells and T-cells;
- B-cells formed in bone marrow and spleen, proliferate upon exposure into anti-body cells or memory cells and multiply increasing defences;
- T-cells released from Thymus, formed 24-48 later to produce apoptosis or stimulate the defence response in cells throughout the body.



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The adaptive system

- Have antigen memory;
- Are antigen specific;
- Principle of vaccinations.

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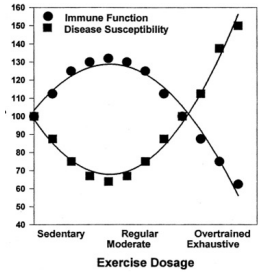
Exercise and immune system



The inverted j hypothesis. Taken from Fairey et al (2002). Physical exercise and immune system function in cancer survivors. Cancer; 94, 2; 539-551.

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Exercise bout

- Reduced lymphocyte and NK (Natural Killer) cell activity up to 6 hours post ex bout with intensity and volume > 90% VO_{2max}, > 90mins;
- Caution to maintain a moderate intensity, with rest between bouts of exercise in cancer patients and rehabilitation.

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Exercise and cancer prevention

- Main sites:
  - Colorectal, breast, endometrial;
- Breast:
  - *European Prospective Investigation into Cancer and Nutrition:*
  - 218,169 pre-menopausal and post-menopausal women ;
  - 6.4 year study;
  - 3,423 incidents of invasive breast cancers were identified. High occupational , household and recreational physical activity were significantly associated with reduced breast cancer risk.

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Breast cancer prevention

- Lee (2003):
  - 20-30% reduced risk.
- Friedenreich and Cust (2008):
  - housekeeping and general recreation had a 21% risk reduction;
  - regular walking 18% risk reduction;
  - Pre-menopausal effects evidence limited, post-menopause significant.

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Prevention

- Colon:
  - 20-25% risk reduction;
  - Mod-vigorous intensity, 30-60mins per day.
- Endometrial:
  - up to 30% risk reduction possible;
  - dose response in 50%;
  - being sedentary risk factor for development;
  - vig. activity, or earlier in life, better than low or later;
  - aim to change behaviour patterns.

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Prevention

- Prostate:
  - Moderate findings (10-20%);
  - Inconclusive evidence, low confidence;
  - Other factors more influential (age, race, history).
- Lung and ovarian
  - Evidence limited and inconclusive;
  - Poor study design;
  - Benefits through behaviour modification and smoking cessation.

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Cancer related fatigue

- Now the most distressing symptom of cancer and its therapies;
- Reported by 60-96% of patients treated by chemo, radio and surgery;
- Can last for up to 12 months post treatment;
- 40% in longer treatment therapies (hormone therapy).

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Cancer related fatigue

- Very debilitating, often affecting the person's will to continue treatment and, therefore, remission chances;
- Causes not fully known, but:
  - anaemia; drugs such as opiates, antihistamines, and anti-sickness medication; electrolyte imbalance; liver failure; steroid withdrawal and sedatives (Thomas, 2005).
- Also:
  - Disturbed sleep pattern, anxiety, depression, nocturia, night sweats and pruritus (itching).

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Physiological Consequences

- Fatigue causes reduced physical activity participation;
- Increased atrophy, exacerbated by inflammatory response seen with tumour growth;
- Myofibril loss, mitochondria reduction, capillary death, reduced P-Cr and enzymes reducing ATP production.

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E-C Coupling

- Ionising radiation interferes with SR impairing C+ offload;
- Tumour itself releases contractile-impairing chemicals;
- Results in reduced ability of calcium offload and re-uptake from SR, inability to re-synthesise ATP and further increased fatigue and slower muscle unit compliance (Lucia et al., 2003).

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Oxygen availability and delivery

- Anaemia;
- Kidney damage;
- Myocardial atrophy;
- Myocardium damage;
- Sarcopenia/atrophy reduces VO_{2max} (↓ a-v O_2 difference);
- Greater reliance on anaerobic pathways.

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Other factors

- Loss of appetite;
- Neurotoxicity, slows motor function;
- Pulmonary toxicity decreases total lung capacity, vital capacity, inspiration capacity and diffusion capacity;
- Hepatotoxicity and Nephrotoxicity affect liver and kidney function and interfere with metabolic activity.

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Exercise and CRF

- Home based unsupervised:
  - RCT show some benefit in home-based PA intervention. Most involve walking or chair-based exercise throughout the chemo/radiotherapy.
- Good compliance rates, but only small reductions in CRF reported.

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Exercise and CRF

- Supervised:
  - Mix of significant (5 studies) and…
  - Non significant (3 studies).
- Good results in prostate patients under-going radiotherapy and ADT;
- Breast cancer: greater reductions in CRF with supervised than home-based.

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Guidance for CRF

- Supervised;
- Low to moderate intensity exercise regimen;
- Regular frequency (3-5 times/week);
- For at least 20mins per session (intermittent, if required);
- Involving aerobic, resistance, or mixed exercise types.

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Relapse statistics

- Livi and colleagues (2007) suggested that 8-10 years after breast therapy 70-80% of patients had not relapsed and recurrence ranged from 4-18%;
- Ovarian cancer, however, is cited as having a recurrence rate of 75% within a few months following therapy (Nandi et al., 2006; Herzog and Herrin, 2011);
- In a study of 88 lung cancer patients, 57% suffered from post-operative relapse (Subotic et al., 2009);
- Following radiotherapy treatment for bladder cancer, there is a 40-50% chance of it returning;
- Colon cancer returns in approximately 40% of those treated, some months or years later.
- Hodgkin's lymphoma has only about 10% recurrence rate.

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Relapse and recurrence

- Irwin et al. (2008):
  - 933 breast cancer survivors;
  - Those who exercised for more than 2.5 hours per week;
  - 67% lower risk of death than controls.
- Holmes et al. (2005):
  - 2987 breast cancer survivors;
  - Walking >3 hours per week;
  - Greater survival and less recurrence than non exercisers.
- Haydon et al. (2006):
  - 526 colorectal survivors;
  - 31% reduced incidence of relapse than non exercisers.

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Exercise, lifestyle and relapse prevention

- Ornish et al. (2005):
  - 93 subjects with early-stage prostate cancer;
  - Refused traditional therapies for PA, vegan diet plus supplementation of soya, fish oils and vitamin C;
  - Reduced prostate specific antigens (PSA) by 4% over 12 months, whilst levels in the control group increased by 6%.
- Holmes et al. (2005):
  - 2987 breast cancer patients;
  - 3-5 hours per week of low to moderate intensity exercise reduced relapse risk compared with those who did < 1 hour per week;
  - Vigorous exercise group for longer showed no greater benefit than low to moderate exercise group, but still greater than < 1 hour per week.

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Factors for relapse

- Stress;
- Socio-economic;
- Poor nutrition;
- Sedentary lifestyle.

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Poverty and obesity

Quispe (2007) found that in the poorest communities of America, where 62% of those studied came from low economic backgrounds, 88% of those were overweight or obese and this had a significant relationship on cancer recurrence, with 69 patients (most of whom came from the 88%) out of 349 studied, relapsing.

It was concluded that patients with a BMI of over 30 had a 20% greater risk of relapse than patients with a BMI of less than 25.

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Mechanisms of benefits

- Thomas and Davies (2007) :
  - ↓ Insulin-like growth factor-1 (IGF1);
  - ↑ IGFBP-3;
  - Need for a range of exercise from formal to dancing.
- Magne et al. (2011)
  - High blood lipid profile (↑ of just 5% influential);
  - Obesity (Holmes et al., 2005);
  - Poor blood glucose profile (diabetes mellitus);
  - 9% relapse reduction after 8 years, in those who lowered their circulating blood lipids.

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Reducing activity

- Irwin (2008) observed an increased risk of death in women who had reduced their activity levels following diagnosis;
  - *Need to continue activity post diagnosis.*
- Meyerhardt et al. (2006):
  - Stage 3 colon cancer (n=823);
  - 47% > chance of survival than sedentary subjects.
- Meyerhardt et al. (2009) showed similar dose effects in male colorectal cancer patients maintaining over 18 MET hours per week of exercise.

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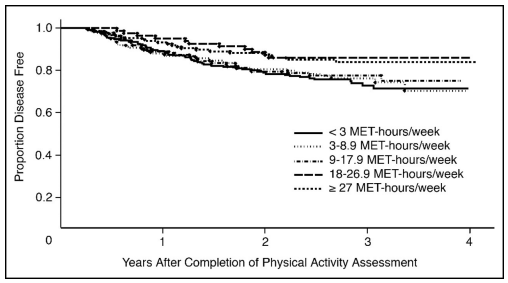

Meyerhardt J A et al. JCO 2006;24:3535-3541

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Psychological health

- Knobf et al. (2007):
  - Many aspects of treatment and coping with disease:
    - Fear
    - Pain
    - Fatigue
    - Negativity
    - Stress
    - Anxiety

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Benefits to psychological health

- Cardiovascular exercise reduces stress hormones and promotes positive ones to give the patient a feeling of well being and motivation. Beta endorphins can ease pain whilst exercising and induce a feeling of euphoria and invigoration.

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Benefits continued…

- Improved self-esteem;
- Improved self-confidence;
- Improved mental alertness;
- Better decision making;
- Improved ability to perform tasks;
- Reduced frustration;
- Increased ability to cope.

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Summary

- Immune system;
- Evidence emerging of prevention benefits;
- CRF: physiological and social (sleep, medications, anxiety, depression, worry);
- Relapse prevention factors: stress, nutrition, <PA, blood lipid and glucose profile, overweightness;
- Psychological health.

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