

Medical Pharmacology

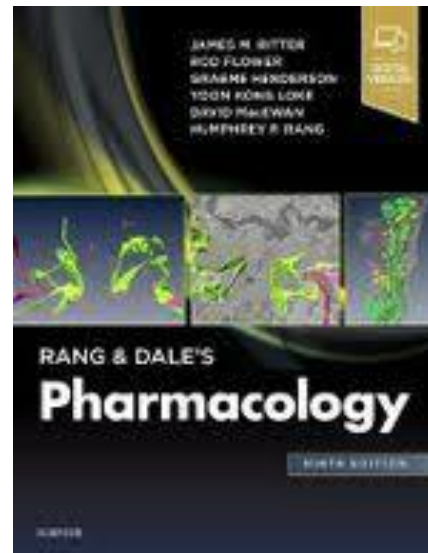


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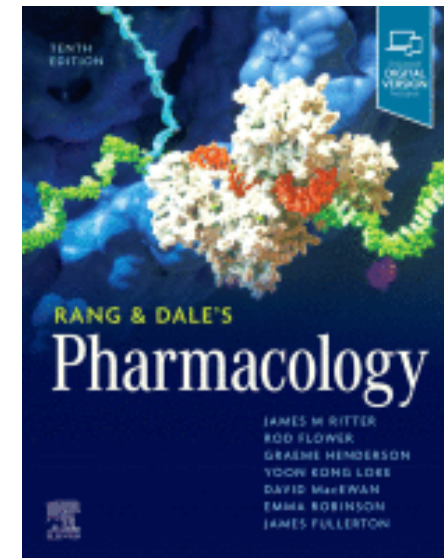


Celebrating
50
YEARS
1970 - 2020

Lecture 5 – management of overweight and obesity



Rang & Dale's
Pharmacology
9th edn 2020
Chaps 31, 33



Rang & Dale's
Pharmacology
10th edn 2023
Chaps 30, 32

COMMONWEALTH OF AUSTRALIA

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Overweight and Obesity

Introduction

- Overweight and obesity resembles the presence of excess storage of fat in the body – an excess body weight for height (high BMI)
- Causes – multifactorial, sedentary lifestyles, lack of regular exercise, ultra processed food consumption, genetic predisposition, drug-induced, and metabolic disorder as well as socioeconomic and environmental determinants
- Risks – greatly increases risk of physical, metabolic, and psychological health problems such as CVD, DM, dyslipidaemia and poor mental health
- Obesity is largely preventable but has become a significant health burden
- At an individual level, effective management of overweight and obesity often needs a multidisciplinary approach including lifestyle modification, behavioural and psychological therapy, weight loss pharmacotherapy and bariatric surgery

Overweight and Obesity – Medicine induced

Medicine classes with examples that commonly cause weight gain

- antipsychotics and mood stabilisers (e.g., haloperidol, chlorpromazine, clozapine, risperidone, olanzapine, quetiapine, and lithium)
- antidepressants (e.g., amitriptyline, nortriptyline, imipramine, paroxetine, escitalopram, citalopram and mirtazapine)
- hormonal contraception
- antihyperglycemics (insulin, sulfonylureas, pioglitazone)
- antihypertensives (beta-blockers)
- Corticosteroids
- anti-epileptics (e.g., valproate, pregabalin, and gabapentin)

Overweight and Obesity – Comorbidities

Patients with comorbidities such as depression and obstructive sleep apnoea may also be obese

- Respiratory – chronic asthma, COPD, sleep apnea
- Cardiovascular diseases
- CNS – stroke
- GI – gallbladder disease, fatty liver, reflux esophagitis
- Osteoarthritis
- Diabetes
- Hormone disorders and more

Overweight and Obesity

Non-pharmacological management

- Preferred - for some patients, lifestyle modification alone may be sufficient to achieve weight loss
- The following points have been found beneficial for weight management if followed properly:
 - ❑ having a meal routine
 - ❑ avoiding processed foods
 - ❑ walking 10,000 steps (equivalent to 60-90 minutes of moderate activity) each day
 - ❑ choosing healthy snacks
 - ❑ choosing healthy drinks (water first and avoid sugary drinks)
 - ❑ learn how to read food labels when shopping and preparing food
 - ❑ be aware of portion sizes
 - ❑ mindful eating techniques
 - ❑ balanced diet with 5 serves of fruit and vegetables per day

Pharmacotherapy for obesity

- **liraglutide / semaglutide**



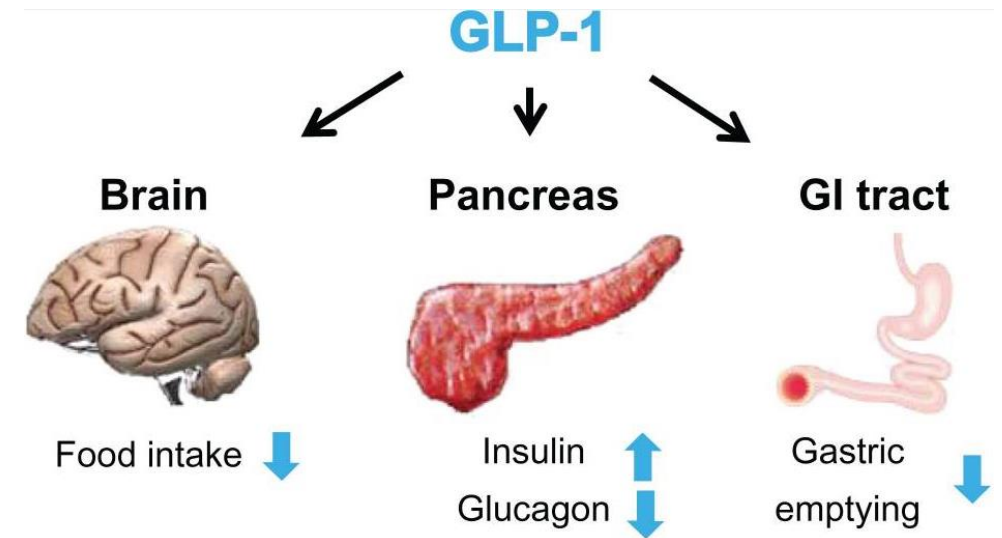
Mechanism of action

- glucagon-like peptide-1 (GLP-1) analogue (see MP week 6)
- originally developed for T2DM treatment, later approved for weight loss treatment
- delays gastric emptying, reduces appetite
- subcutaneous injection

Adverse effects / precautions

- nausea, vomiting, diarrhoea etc, increased risk of cholelithiasis

- Note that pharmacotherapy should be used in conjunction with lifestyle mods





Diabetes Australia stands up for people with type 2 as Ozempic shortage hits Australia

Joint statement: Prioritisation of semaglutide (Ozempic) supply for people with type 2 diabetes during shortage

17 May 2022

Novo Nordisk Pharmaceuticals Pty Ltd, the sponsor of semaglutide (Ozempic) solution for injection pre-filled pen, notified the Therapeutic Goods Administration (TGA) of a shortage of both strengths of semaglutide (Ozempic) products due to an unexpected increase in consumer demand. The increased demand is due to extensive prescribing for obesity management, for which Ozempic is not indicated. The shortage is significantly affecting people using Ozempic for its approved use for type 2 diabetes.

This statement has been developed by the TGA and:

- The Australian Medical Association (AMA)
- The Royal Australian College of General Practitioners (RACGP)
- The Australian Diabetes Society (ADS)
- Diabetes Australia (DA)
- Pharmaceutical Society of Australia (PSA)
- The Pharmacy Guild of Australia
- The Society of Hospital Pharmacists of Australia (SHPA)
- National Pharmaceutical Services Association (NPSA)
- Novo Nordisk Pharmaceuticals Pty Ltd.

To prioritise essential continuity of care for people with type 2 diabetes during the shortage, health professionals should limit prescribing and dispensing of semaglutide to its approved use:

Pharmacotherapy for obesity

- **orlistat**

Mechanism of action

- reversible GI lipase inhibitor
- forms covalent bond with active serine residue of gastric & pancreatic lipases
- inactivated lipase unavailable to hydrolyze triglycerides into absorbable free fatty acids and monoglycerides
- inhibits dietary fat absorption by approximately 30%
- main effect results from patients decreasing fat intake to avoid resultant effects such as flatulence with discharge, faecal incontinence, fatty oily stools etc

Adverse effects

- decreased absorption of fat-soluble vitamins
- contraindicated in pregnancy



Pharmacotherapy for obesity

- **phentermine**

Mechanism of action

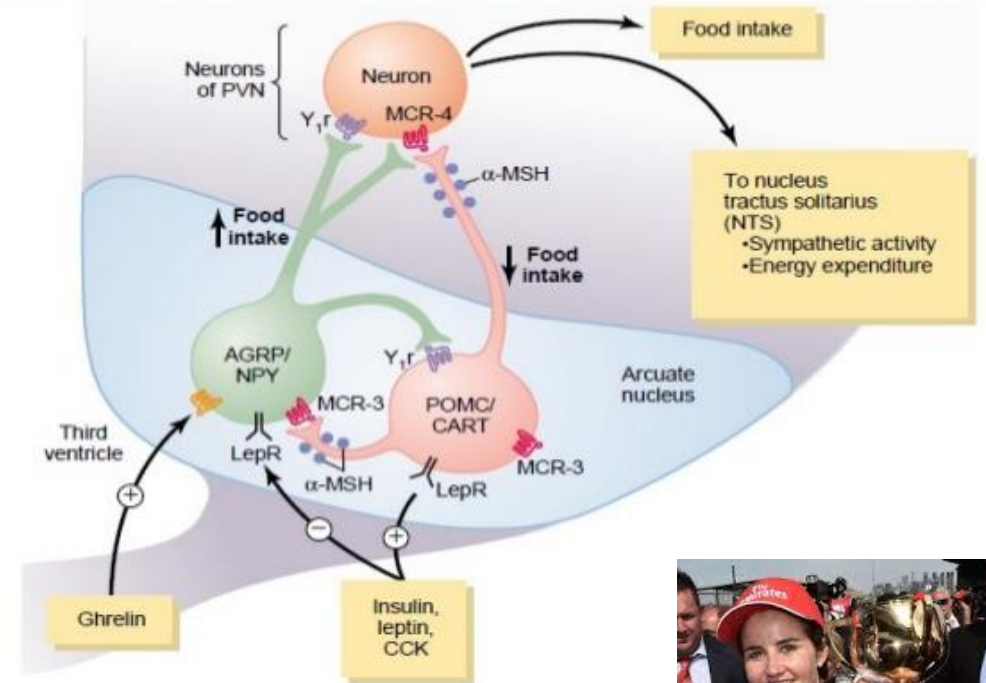
- appetite suppressant
- indirectly-acting sympathomimetic
- increases NE release in lateral hypothalamus, which in turn inhibits neuropeptide Y - key stimulator of food intake
- also increases resting energy expenditure

Adverse effects / precautions

- CNS stimulation, headache
- contraindicated in CV disease, hyperthyroidism, drug misuse, BPH, epilepsy, MAO inhibitors

- Note that pharmacotherapy should be used in conjunction with lifestyle mods

Neuron And Neurotransmitters In The Hypothalamus That Stimulate Or Inhibit Feeding



Pharmacotherapy for obesity

- Bupropion and naltrexone
 - The combination is believed to cause a reduction in appetite and increase in energy expenditure by increasing the activity of pro-opiomelanocortin (POMC) neurons
 - Bupropion increases dopamine activity in the brain, which appears to lead to a reduction in appetite and increase in energy expenditure by increasing activity of POMC neurons.
 - Naltrexone blocks opioid receptors on the POMC neurons, preventing feedback inhibition of these neurons and further increasing POMC activity.
- **Other off-label medications**
 - Methylphenidate
 - Zonisamide
 - Octreotide etc