



## Plenary 1: Weight control

### Themes

- Homeostasis
- Host defences
- Lifestyle factors
- Health promotion and disease prevention

### Panel

- Rosemary Stanton: nutrition and health specialist
  - Main concern for public about weight is appearance and body image, **not health**
  - Diets often work in the short term but not the longer term
    - People are complicated, many factors that determine adherence
  - Genes haven't changed but diet and lifestyle have
    - Pregnancy is an important stage for potential weight gain
- Andrew Moorhouse: physiologist
  - Weight control is a very complex issue
    - Not as simple as calories in = energy out
    - Intervention studies need rigorous standards
      - Critical evaluation is important
- Pharmacologist
  - Estrogen regulates fat metabolism and appetite
    - Menopause is important
  - Central adiposity is associated with high cardiovascular risk, thus the health impact of obesity is important
  - Emotion and food intake are related
    - Humans are influenced by stress, food is an emotional release
  - Obesity is a major reason for non-compliance to drugs
    - GPs are important for support
- Dietician nutritionist
  - Kidney disease is related to obesity
  - Need to eat to survive, but eating is also a social activity
  - Education is important, obesity is a multi-disciplinary problem

## SG 1

### Plenary

- Perceptions of body image
  - Unrealistic, peers, genes, media
  - Gender: male – strong, drinking, female – thin, sexy
- Diet and food
  - Overeating, portions
  - Time, price
  - Social pressures
  - Kids TV, ads
- Culture
- Age and hormones
  - Women, menopause

### Diets and dieting

- Healthy diet vs weight loss
- Metabolism
  - Genes, gender
  - Body programming – eating breakfast, when, how much eaten each meal
  - ?weather – cold, eat more?
- Special diets, allergies
- Yoyo effect (weight up and down)
- Sustainable diet
- Time of day
- Snacks
- Egs: south beach, atkins (high protein, low CHO), weight watchers, lemon detox, jenny craig, sureslim

### Clinical trials – things to look for

- Large sample
  - More representative – external validity
  - Internal validity (power) increases with sample size
  - May show a significant small difference between two groups better
- Blinding
- Bias – the systematic introduction of error into a trial that distorts the final results
  - Eg. sampling/selection bias
- Selection of sample
- Intervention
- Measurement/observation
- Short-term/long-term measurements, timecourse

### Biases

- Population, selection (subjects and source), allocation
- Confounding factors
  - Intervention → → confounders (eg. age, gender) → → outcome
- Experimental problems
- Measurement of outcomes
- Loss to follow-up → can use intention to treat

### Anti-bias

- Careful selection criteria (inclusion/exclusion)
- Randomisation
- Baseline assessment and comparison

## NHMRC guidelines

### Summary

- Enjoy a wide variety of nutritious foods
- Eat plenty of vegetables, legumes and fruit
- Eat plenty of (wholegrain) cereals: bread, pasta, rice and noodles
- Include lean meat, fish, poultry, etc
- Include milk, yogurt, cheese (reduced fat)
- Drink plenty of water
- Limit saturated fat and moderate total fat intake
- Choose low-salt foods
- Limit alcohol
- Eat moderate amounts of sugars and foods with added sugars
- Maintain a healthy body weight by being physically active and eating according to activity
- Care for food: preparation and storage
- Infants: breast feed

### Fruit and vegetables

- 5 servings of vegetables, 2 of fruit everyday
  - Eg a serve: 75g (half a cup) of cooked or green leafy vegetables, 1 cup of salad or a medium potato
  - Eg a serve: medium apple, banana, orange, pear, cup of diced pieces of fruit or canned fruit

### Cereals

- Grains like: rice, oats, corn, breads, breakfast cereals, pasta, noodles, flour
  - Women: 4-9 serves/day
  - Men: 4-12 serves/day
  - Number should be in relation to level of physical activity
- One serve: 2 slices of bread, 1 cup porridge/bfast cereal, 1 medium bread roll, 1 cup of cooked pasta, rice, noodles

### Fats

- Australians eat a lot of fat compared to the world
  - Total fat (saturated, monounsaturated, polyunsaturated) makes up 1/3 of total food energy intake of Australian adults
    - Total fat should make up only 20-25% of food energy intake
- Saturated fats can increase our risk of heart disease and other diseases
  - Current intake in Australia is 12.5% of total energy intake, 10% recommended
  - Sources: cheese, butter, cream, meat, chocolate, potato chips
- Companies hydrogenated unsaturated fats into saturated fats to help with storage and reheating

### Sugar

- Sugars improve the way food tastes and are added to many foods
  - High levels of refined sugars are energy dense and have lower levels of other nutrients
- Food high in sugar can displace other more nutritious foods
  - NHMRC recommends no more than a moderate level in our diet
    - Added sugar should be no more than 10% of energy intake (about half current Australian intake)

### Calcium

- Sources: milk and foods produced from milk: cheese, yogurt
  - Non-dairy sources: almonds, salmon with bones, calcium fortified soy
- Calcium is a mineral important for healthy bones throughout life, especially to prevent thinning of bones in later life
  - Women: 2-3 serves of milk, yogurt, cheese/day
  - Men: 2-4 serves/day
- 1 serve is 1 cup of milk, 200g of yogurt, 40g of cheese (2 slices)

### Iron

- Particularly important in girls, women and vegetarians
- Deficiency can cause fatigue, listlessness and can lead to anaemia
  - Advised 65-100g of lean red meat 3-4 times/week

### Exercise

- Eat according to energy needs
  - Total of 30 minutes of moderate physical exercise on most (pref. all) days of the week
    - Doesn't have to be organised exercise, can be household chores, or just being active

Clinical

- Symptoms of GI disease
  - Vomiting, hematemesis
  - Diarrhoea
  - Constipation
  - Abdominal pain/chest pain
  - Flatulence, bloating
  - Bloody stools/abnormal stools
  - Nausea
  - Cramps
  - Weight loss
  - Anorexia
- Signs of GI disease
  - **Abdominal tenderness**
  - **Masses**
  - **Distension (fluid)**
  - **Jaundice**
- Kidneys:
  - Hematuria
  - Loin pain
  - Nocturia
  - Dysuria
  - Frequency
- Eg. Diarrhoea characterising the presenting complaint:
  - Onset, frequency, consistency
  - Appearance – blood, colour, mucus
  - Past episodes, contacts
  - Associated symptoms
  - Triggers, relievers
  - Travel
  - Treatments
  - Impact on life, other concerns

Examination

- Observation – from above and at the level
  - General
  - Pallor/jaundice
  - Scars
  - Distension
  - Masses
- Palpation
  - Superficial/gentle
    - Looking for tenderness
    - Process:
      - ‘Are you sore anywhere? Do you mind if have a feel, let me know if it’s uncomfortable at all’
      - Palpate with edges of fingers, watch person for flinch
        - Cover all areas by quadrants or other method:
          - Quadrants: umbilicus division, left right upper and lower
          - Other: bottom of ribs, iliac crests, midclavicular lines
            - Epigastrium, LR hypochondrium, LR iliac fossa, LR lumbar, umbilical, suprapubic
  - Deep
    - Looking for masses
    - Process:
      - Same but more strongly, be aware of rectum muscles that are not masses
- Liver:
  - Normally 5<sup>th</sup> rib to costal margin
    - Feel for enlargement / ?rydell’s? lobe
  - Palpate from below, lateral to rectus muscle
    - Get patient to breathe in and out, feel for movement of liver
    - Palpate more laterally
- Percussion
  - Percuss from below to costal margin, hear resonant to dull sound
    - Observe changes on breathing
  - Percuss from top down, observe changes on breathing
    - Estimate size of liver

## SG 2: Wide world of diets

### Scenario

- 50 year old male presents to GP
  - DM, HBP
  - Overweight for most of adult life – 100kg, 170cm (BMI: 34.6)
    - Waist 112cm
  - Tried a few diets, wants a new one
- Tests:
  - Diet
  - Exercise
  - Blood test – hypothyroidism, Cushing's
- Actions
  - Refer to dietician

### Measurements

- BMI
  - Weight (kg) / height (m)<sup>2</sup>
  - Levels:
    - Underweight: <18.5 kg/m<sup>2</sup>
    - Normal: 18.5-24.9
    - Overweight: 25-29
    - Obese: 30+
    - Vary with ethnicity and can be controversial
- Waist measurement
  - Measures central adiposity – visceral fat: liver, kidneys, gut, omentum
  - BMI >25, problem if: waist >102cm (male), >88cm (female)
- Waist-hip ratio
  - Ideally: <0.95 (male), <0.8 (female)

### Diets

- Atkins
  - High protein (15% energy)/fat (65%) → unmoderated
  - Changes lipid profile
    - Not good for people at risk
  - 65% of people drop out
  - Effectiveness:
    - Good short term effectiveness, moderate long term effectiveness
    - Not healthy, hard to follow
- Weight watchers
  - Points system + group meetings
    - Good short term and long term effectiveness
    - Quite healthy and easy to follow
- Slim fast
  - Shakes, meal replacements
    - Good short term effectiveness, bad long term effectiveness
    - not healthy (liquid meals), hard to follow – unpalatable
- Rosemary Conley
  - Exercise class and low fat diet
    - Good short term effectiveness and long term effectiveness
    - Very healthy and very easy to follow
- Zone
  - Low carb, low fat. Ratio: 40:30:30 protein:carb:fat
    - Not very good short or long term effectiveness,
    - Quite healthy, hard to follow (have to measure portions etc)

- Ornish
  - High carb, less than 10% of energy from fat
    - Good short term and long term effectiveness
    - Quite healthy, hard to follow – hard to keep fat out of diet
- LEARN
  - Low fat, high carb (55-60%), exercise recommendations, calorie restrictions, behaviour modification
    - Good short term and long term effectiveness
    - Very healthy, hard to follow
- CSIRO
  - Less carbs, more protein, less fat
    - Good short and long term effectiveness
    - not very healthy or easy to follow

#### Key points

- Hard to say one diet is good and another bad
- Diets are for the long term → need to either teach good habits or provide long term benefits

#### Key weight loss strategies

- Physical activity
- Decreased calories/kJ and fats
- Breakfast
- Self-monitor and check own weight regularly
  - Possibly have another person monitoring you
- Consistent eating patterns
- Catch slips before they become large regains
- **Initiating weight loss after a medical event is more effective → motivation is high**

Good and bad foods

- Trans fats
  - High in energy
  - Increase LDL, and decrease HDL cholesterol
  - Affect cell membranes:
    - Cell membranes are the site of interaction of cells with the rest of the body
    - $\Omega 3$  fats increase the fluidity of the membrane increasing receptor activity
    - $\Omega 6$  fats and trans fats make the cell membrane more rigid, and thus less functional
- Good fats
  - Poly/mono unsaturated fats
- Cholesterol
  - Sources: red meats (not vegetables)
    - Vegetables contain plant sterols that compete with cholesterol for uptake and decrease bad cholesterol in blood
- Salt
  - Dietary salt: 120mg/100g of food is high
  - High amounts of salt causes hypertension
- Sugar
  - Increases insulin (pancreas)
    - Increases fat deposition
  - Glucose
    - Has an osmotic effect – diuresis
    - Glycosylation of blood proteins
    - Microvascular occlusion

Old vs young

- Do less exercise
  - Reduced exercise and stress have hedonic value
    - Stress causes us to eat more (especially fatty foods)
    - Many people eat to feel good
- Have lower muscle mass
- Have a lower basal metabolic rate

Articles

- **Mindless eating: Wanskin & Sobal**
  - Food decisions – how many do we make?
    - Decisions include: what, how much, when, where, who
  - People thought they made ~15 decisions, actually estimated to make 226 (confirmed by 3 counters)
    - I.e. most people don't realise how many decisions they make or how complex eating is
  - Food decisions were related to BMI in a U-shaped curve
    - Normal weight and obese made more food decisions than overweight
      - Thought that they both thought about food, but normal had more 'no' answers
    - Notice: underweight people are even more preoccupied with food (more food decisions)
  - People were given exaggerated meal sizes
    - In those with the big bowl, they were asked if they thought they ate more/less/same than normal
      - Many did not chose correctly
      - Of those who chose correctly, they were asked why they did
        - Only 4% answered they did because they were influenced by the study vs 'hungry', 'it was free'
    - Shows that we are unaware of how much we eat and that we often just eat because it's available



- **The ecology of eating: Rozin, Kabnick, Pete, Fischler and Shields**
  - France vs US (France has lower BMI, but they eat more saturated fats and total fats) – French paradox
  - Compared:
    - Portion sizes (US larger)
    - Speed of eating (French longer – better appreciation of food, eating experience)
    - Cook books (US books had larger serving sizes)
    - Supermarkets (US had larger sized servings of foods)
    - All you can eat restaurants (US had many more)

## Videos

- Video 1:
  - If you watch how much you eat, and see how much you eat, you eat less
    - Eg. if unlimited chicken, bones removed vs bones not removed – bones not removed ate less
- Video 2
  - Popcorn
    - The more popcorn you're given, the more you eat (even if stale)
    - Thus, the greater the portion, the more we eat
- Video 3:
  - Summer school
    - 120g pasta, 85g meat
      - If we double the serving size, kids still eat
        - 73% more eaten with larger servings
    - Factors:
      - Environmental influence of peers
      - Portion size altering amount eaten
- Video 4:
  - Eating in front of the TV vs at the dining table
    - Initially change to dining table had no difference in rate etc
    - Then, once full at the dining table, kept eating at TV (ie. after stomach indicated fullness)
      - TV distracts from eating and satiety
- Video 5:
  - Pain free weight loss
    - Adiposites can swell 1000x with fat
    - **Tip 1: protein is the most satisfying nutrient**
      - Lean protein such as: fish, beans, tofu, skinless chicken
      - Decrease snacks, increase fruit and vege
      - Calcium – reduces fat absorbed in gut
    - **Tip 2: portion size**
      - Distracted = overeating. Eg. social situation, variety = over eating
      - Food diary – allows you to notice what you're eating
    - **Tip 3: keep things simple reduce variety**
      - Drinks – water instead of alcohol
        - Water stretches stomach, makes you full
        - Good alternative to food is soup: water with food
    - *Idea is to modify diet while keeping choice and preference*

## *Hospital 1*

### Gastro/general history

1. Introduce yourself and consent
2. Demographics – name/age/location/occupation
3. Presenting complaint – how long, what
4. History of presenting complaint
  - General things:
    - i. Onset
    - ii. Characterise pain – dull, sharp, burning
    - iii. Location (site)
    - iv. Aggravating/relieving
    - v. Radiation
    - vi. Associated symptoms
    - vii. Severity (\* /10), function
  - PQRST acronym
    - i. Position
    - ii. Quality
    - iii. Radiation
    - iv. Severity
    - v. Timing – onset, duration, frequency
    - vi. Associated symptoms
5. Past medical history – what diseases, how long, treatment
6. Medications – what dose, how long
7. Allergies – what, reaction
8. Family history – what, who, age
9. Social history
  - Smoking – now, how much, how long (pack years)
  - Alcohol – how much, how often
  - Diet + exercise
  - Living arrangements – who, will they care for you?, ADL
10. Systems review

Non-diet approaches to weight loss

Non-diet method	Success rate	Suitability	Side effects	Compliance	Contra-indications	Cost
Behavioural approaches: strategies such as self-monitoring, and identifying what to change and how	Good short term, and long term	Also improves health outcomes	Depression if don't reach goals	Found hard to change routines initially	Need high levels of motivation, honesty Need trust Need to keep records and follow up	Cheap or inexpensive, different options
Exercise	Good with good diet Improves health even if no weight loss	Everyone can exercise to some degree	+ve effects – WL, decreased CVD risk factors, decreased BP, decreased chol, decreased triglycerides, increased HDL, decreased serum glucose, increased antioxidants -ve – strain muscles/ligaments, fatigue, soreness	Generally quite good in studies, however these may have high motivation	Recent MI, Hx cerebrovascular, kidney/liver disease, cancer, pregnancy, DM, high risk MI	Minimal, gym membership?
Surgery: gastric restriction, intestinal malabsorption, laparoscopic gastric banding	Good success	Severely overweight Risks so high that surgery risks are better Exclude all other options first BMI>40, psychologically stable etc	Nausea, vomiting, dehydration, dumping syndrome, bowel habits, constipation, pregnancy	Before: no binge eating, smoking/alcohol After: diet, food diary, exercise, support groups, success rate high	Substance abuse, Hx non-compliance, antipsychotics, illness, low life expectancy	\$12000, medicare
Pharmacotherapies: sibutramine, orlistat, phentermine	Shown quite effective if also change lifestyle, have to stay on drug	BMI>30, more drastic, >27 if risk factors	Dry mouth, constipation, insomnia, increased BP, HR, etc Fatty/oily stools, vitamin deficiency	Side effects important	Many: HBP, HD, anorexia, pregnant	Expensive – not worth it unless high risk
Magic bullet: Hoodonia gordonii, P57 – steroidal glycoside from south Africa	No trials published, thought to decrease food intake Probably TGA listed	Still testing, affects liver function	Liver interference (damage?) Liver important in drug metabolism, enzyme may cause inhibition of enzymes/induction of enzymes changing other drugs pharmacokinetics	By itself it is easy/effortless, SE?	Extreme exercise, liver disease, diabetes, meds – interactions, relatively new (2004), no scientific research, long term SE unknown	\$65 AUD, for 80 tablets

*Overall: Different therapies are suitable to different people – need to keep all options in mind*

*Note: people are fat because – environment/lifestyle, emotional satisfaction of eating (even though no one wants to be fat)*

## *Ethics tutorial*

### Public health ethics

- The best health possible for everyone – links to communitarianism and utilitarianism
  - EG: surgical waiting lists
    - Tend to discriminate in terms of age, smoking, weight

### Debate

- That it is valid for the medical profession to give overweight people a lower priority on surgical waiting lists
  - Public health point of view – greater good for greater number of people
    - Medical problems – risks during surgery, recovery time, encourages good health
  - VS: discrimination, can we discriminate in terms of 'genetics, SES, etc'

Article: Gut hormones and the regulation of energy homeostasis Murphy and Bloom

- Energy balance is a homeostatic system
  - Obesity may be the result of this regulatory system not being able to cope with the societal changes of the western world
  - Regulated by the brainstem and hypothalamus
    - Neural and hormonal signals from periphery
- Hormones:
  - **See handout sheet with summary**
- Central appetite circuits
  - Precise mechanisms of central action are unknown or contentious
  - Arcuate nucleus is important for integrating peripheral circuits
    - Expresses NPY, AgRP, POMC
  - Paraventricular nucleus is a target for ARC neurons
    - Signals to higher brain centres and the SNS and the thyroid axis
  - Vagus nerve is important afferent track
- Gut hormones on energy homeostasis
  - Satiety is probably a cumulative effect of a number of submaximal gut hormone responses
    - Ie. gut hormones have an additive effect on appetite
  - Hunger, satiety and nausea are thought to exist on the same spectrum
- No effective drugs have been yet discovered
  - Bariatric surgery is the current most effective treatment
    - Problems with cost and associated mortality
- Physiological and pathophysiological roles of gut hormones in energy balances is yet to be defined
  - May play an important role in pharmacological therapies of the future

## Eating fish and chips – different perspectives

- **Methadone**

- Causes constipation
  - Fatty foods would not help this
- Fat in diet could also lead to increased bacteria → bloating
- Haemorrhoids from straining
- Social factors
- Effects are more long term than short term

- **Malnourished alcoholic**

- Short term:
  - Alcohol impairs nutrient absorption by damaging the lining of the GIT
    - Prevents absorption of nutrients – protein, fats, carbs, salt
- Long term
  - Liver failure – bile not produced, fat absorption impaired
  - Pancreas damage – malabsorption: enzymes for digestion not produced, diabetes – insulin not produced

- **Coeliac disease**

- Gluten intolerance, autoimmune disease where the protein gluten is not broken down
  - Causes an inflammatory response in the intestine that damages the villi
    - SA of villi decreases and absorption is impaired
- Overall it is an immune reaction to longer peptides that are taken up by transglutaminase
  - Antibodies are formed to the food and the transformed food and cause an inflammatory response
- Gluten is found in: wheat, rye, barley, oats
  - Intolerance vs allergy – longer term (spectrum of intolerance occurs)
- Fish and chips
  - Potato, wheat batter on chips problem
    - Short term – bloating, abdominal pain, vomiting, fatigue, breathlessness, **diarrhoea**
    - Long term – anaemia (Fe absorption), osteoporosis (Ca absorption), weight loss, irritable bowel syndrome, depression (tryptophan converted serotonin/NAD), bowel cancer, obesity (lack of choice)

- **Gall bladder removal**

- Stores bile
  - Bile salts – emulsify fats, polypeptides (lecithin) – emulsify fats
  - Functions – transport fats as micelles and give lipases access to fats for digestion
- Short term – diarrhoea, bloating, smelly stools, abdominal pain
- Long term – malnutrition, fat not absorbed
  - Change gut flora → smelly stools

- **Long term diabetic**

- Chips – starch, carbs. Potatoes – high GI, high in glucose
  - Short term – hyperglycaemia
    - Glycosylation of blood, thicker, stickier
      - Microvascular occlusion
  - Long term – HD, obesity, CVD, cholesterol
    - Decreased healing rate → small vessels blocked, restricted blood flow

### Obesity - complications

- Diabetes
- Hypercholesterolaemia
- CVD
- Sleep apnoea
- Cancers – breast, colon, pancreatic
- Hypertension
- Endocrine – polycystic ovary
- Osteoarthritis
- CeVD
- Anaesthetic risk
- Aggravation of skin conditions – eczema
- Immunity problems – infection

### Type 2 Diabetes mellitus - complications

- Chronic renal disease – diabetic nephropathy
- Retinopathy
- Neuropathy
- CVD, CeVD, PVD
- Infection – wound infection
- Poor wound healing

### T2DM risk factors

- Genetics!
- Inactivity
- Obesity
- Diet

### Psychosocial history

- Lifestyle
  - Smoking, alcohol, drugs, diet, sex, exercise
- Home
  - ADL, circumstances, relationships, access
- Activities
  - Job, pets/animal exposure, travel, hobbies
- Personal
  - Beliefs about illness (pick up in conversation)
  - Cultural, religious beliefs
  - Financial situation, stressors/coping methods

### Gastro psychosocial history

- Focus on:
  - Diet, alcohol, drugs
  - ADL, home situation, relationships, access
  - Travel (hepatitis, gastro), pets, job

### Smoking, alcohol, drugs

- Smoking
  - Do you smoke? What do you smoke, how much do you smoke? → pack years
  - Have you ever smoked?, how long?
- Alcohol
  - How much do you drink everyday?
  - Alcohol audit
- Drugs
  - Recreational
  - [www.whitehousedrugpolicy.gov/pdf/street\\_terms.pdf](http://www.whitehousedrugpolicy.gov/pdf/street_terms.pdf)

## Examination

- Spleen
  - Location
    - Below lower left rib, around the L margin of the 8<sup>th</sup> intercostal space
    - Lateral to the anterior axillary line
  - If it can be felt, it is 2x normal size
  - Examination:
    - Palpate with R, L supporting under ribs
      - Palpate up from the left lower quadrant on inspiration
      - Feel with finger tips for edge of spleen
      - Lift left side and palpate again
    - Percuss the 9<sup>th</sup> intercostal space – should be resonant
- Kidney
  - Location
    - T12-L3
  - Examination
    - Place R hand at back between rib cage and vertebrae
    - Palpate with L hand lateral to rectus muscles at costal margin
      - Belotte kidney with inspiration
- Ascites
  - Gas is resonant, liquid dull
    - If there is fluid in the peritoneal cavity – fluid goes to the side when lying down and gas in the middle
  - Percuss abdomen medially to laterally listening for resonance/dullness
  - Shifting dullness
    - If dullness is found, have patient lean towards you and see if area that is dull moves
- Auscultation
  - Listen for normal bowel sounds
    - Centrally, 30s
  - Bruits (shh shh shh)
    - Aortic – listen at the midline above umbilicus
    - Renal – listen 2.5cm either way

## Communications

- Alcohol complications
  - Malnutrition
  - Stomach ulcers
  - Pancreas
  - Heart
  - Lungs – TB?
  - GIT inflammation
  - Nervous system – loss of sensation
  - Neurological issues – memory confusion
  - Neurological damage
  - Psychiatric
  - Hypertension
  - Muscle loss
  - Impotence
  - RBCs
  - Skin – flushing, sweating, bruising
- Standard drink
  - 10g alcohol = 285ml beer (middy) = 120ml wine (small glass) = 30ml spirits (shot)
- Alcohol dependency audit – see sheet

## Motivational interviewing

- Assess willingness to change
  - Good/bad things about drinking – social, relax, taste, health, embarrassment, vulnerable, photos
  - Good/bad things about not drinking – save money, control, help others, social isolation
- Put information together for patient – summarise
- Get them to think of ways they can change → small changes



**\*\*SEE TUTORIAL HANDOUT\*\***

Problem A

Step	NADH	FADH <sub>2</sub>	ATP equivalent	
Glycolysis: glucose → 2 pyruvate	2		5 + 2 ATP	
2 pyruvate → 2 acetyl-coA	2		5	
2 Acetyl-CoA → CO <sub>2</sub>	6	2	15 + 3 + 2 GTP	
				Total ATP = 32 32/180 = 0.178 molATP/g

Step	NADH	FADH <sub>2</sub>	ATP equivalent	
C 18 Stearate → stearyl-coA			-2	
Beta-oxidation: steryl-coA → 9 acetyl-coA	8	8	20 + 12	
9 Acetyl-coA → CO <sub>2</sub>	27	9	67.5 + 13.5 + 9ATP	
				Total ATP = 120 120/284 = 0.423

Step	NADH	FADH <sub>2</sub>	ATP equivalent	
Glycerol → DHAP	1		-1 + 2.5	
DHAP → PYR	1		2.5 + 2ATP	
PYR → Acetyl CoA	1		2.5	
Acetyl CoA → CO <sub>2</sub>	3	1	7.5 + 1.5 + 1 GTP	
				Total ATP = 18.5 18.5/92 = 0.201

NOTE: NADH in the cytoplasm to be used needs to be moved into the mitochondria

Mechanisms: shuttles

Malate aspartate etc shuttles are fine

Glycerol-DHAP shuttle converts NADH to FADH<sub>2</sub> and thus has a lower energy yield

NOTE: beta-oxidation occurs in the mitochondria, synthesis is in the cytosol

Problem B

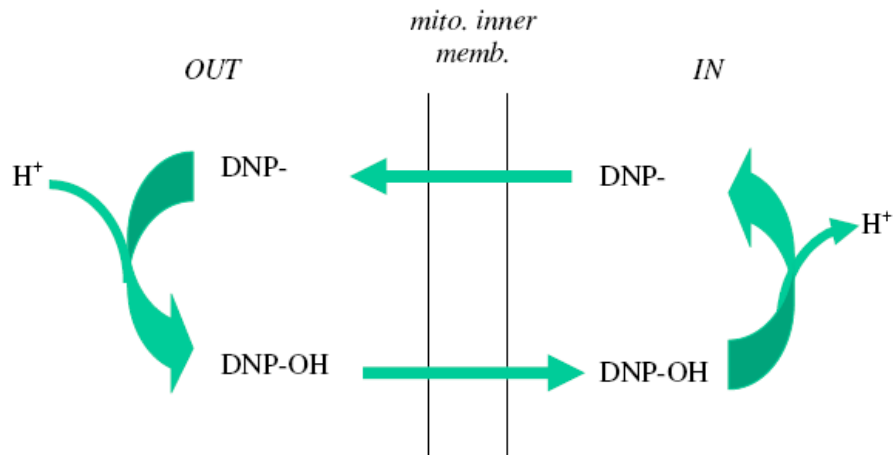
- Thiamine deficiency results in inactivity of the TCA cycle and glycolysis pathways
  - Deficiency means enzymes have decreased activity (PDH, alpha-ketoglutarate dehydrogenase)
  - Problems in:
    - Actively respiring muscle cells, heart, brain → aerobic pathway blocked
    - Can often result in cardiomyopathy, fatigue
  - EG diseases:
    - Berri Berri (dietary deficiency), Wernicke-Korsakoff syndrome (alcohol-related) – neurological problems

Problem C

- Carnitine transport system
  - Fatty acyl-CoA is not transported into the mitochondria
    - Inactivates beta-oxidation – thus, not breakdown of fatty acids
  - Affects:
    - ATP supply to skeletal muscle
    - Liver/heart are less affected – constantly working and carnitine transport is not rate-limiting
  - May result In hypoglycaemia – glucose used instead of fat
- Severe form can present in infancy (<10% activity)
  - Deposition of fat to the liver (hepatomegaly) and cardiomyopathy
  - Hypoglycaemia, hypoketosis

### Problem D

- DNP uncoupling protein
  - Dissipates pH gradients by picking up a hydrogen ion and taking it across the membrane
- Respiratory chain needs a  $H^+$  gradient for production of energy
- Application for weight loss:
  - People can eat, and generate heat, but not energy (ATP)
    - Thus the body works harder to produce energy
  - Unfortunately, people died because they lost too much energy such that vital organs could not be supplied



## Nutrition groups with special needs

### **Anaerobic/strength sports person**

- EG: weight training, running 100 metres
  - Energy is from ATP and then creatine phosphate then muscle glycogen
- Potential problems
  - If all ATP is used up, cell death
- Diet
  - High carbohydrate diet
  - After exercise – high GI carbohydrates, sports drinks for high glucose uptake
- Supplements
  - Multivitamins
  - Creatine
  - Protein supplements for muscle building
  - Glutamine

### **Aerobic/endurance sports person**

- EG: running a marathon
  - Uses muscle glycogen via TCA cycle
    - Then uses liver glycogen
    - Then release of free fatty acids from adipose cells
    - Then protein breakdown of muscles
- Potential problems
  - Heat generation, exhaustion
  - Can exhaust glycogen stores
  - Cramps
  - Hydration
- Diet
  - Nutrition dense foods
  - Fibre, fruit
  - Moderate amount of proteins
  - Water
  - Carb loading
- Supplements
  - Multivitamins
  - Chromium
  - Carnitine
  - Deer antlers

### **Adult insulin dependent diabetic**

- Potential problems
  - Polydipsia, polyuria, polyphagia, decreased immune function, increased healing time, ketoacidosis, seizures, coma, dehydration
  - Retinopathy, neuropathy, heart problems (atherosclerosis), nephropathy, infection, poor wound healing
- Diet
  - Shouldn't eat: sugary foods, too much salt
  - Eat: lean meats, low fat foods, low cholesterol, fish 2-3x/week, fibre, vegetables, fruits, low GI foods,
- Supplements
  - Vitamin E, C, B12, Biotin, Mg, Zn

## Coeliac disease

- Potential problems
  - Anaemia
  - Osteoporosis
  - Depression
  - Bowel cancer
  - Weight loss (FTT)
  - Obesity
- Diet
  - Don't eat gluten – wheat, rye, barley, oats and their products
  - Need gluten free products
- Supplements
  - Iron
  - Calcium

## Vegan

- Potential problems
  - Deficiencies: Ca<sup>2+</sup>, Iodide, Fe, Vitamin B12, D, omega 3 fatty acids
  - Anaemia, osteoarthritis
- Diet
  - No animal products
  - Need proteins from alternate sources:
    - Legumes, nuts, tofu, lentils, walnuts, omega 3
- Supplements
  - Fe, Ca, V B12, D, Iodine
  - Depends on balance of diet

## NHMRC guidelines

- Potential problems
  - Preparation
  - Cost
  - Motivation
- Diet
  - Lots of veges, fruit, legumes, wholegrain cereal
  - Some meat, fish, poultry, dairy
  - Little saturated fat, salty foods, processed foods with added sugars and fats, high GI food, alcohol
  - Moderate total fat intake
- Supplements
  - Vegetarians: VB12, omega 3 fatty acids (walnuts), Ca (Ca fortified soy), iron

## Notes:

- Omega 3 – low in current population
  - Deficiency can cause depression, decreased cognitive function
- Omega 6 – relatively high in population
  - Found in corn/sunflower oil
  - Easy to produce – chips, biscuits etc
  - Better preserved

## Biochem quiz

- Dietary FA → TAG
  - Humans cannot convert FA → glucose or glycogen
- TCA cycle –limited by the rate at which NADH and FADH<sub>2</sub> are reoxidised
  - I.e, based on O<sub>2</sub> and ADP
- Sugar levels /gram
  - Nutri-grain>icecream
- Rate of ATP turnover: Brain > heart
  - 20% vs 11%
- Alpha cells produce glucagon
- Glycogen stores, skeletal muscle has 2x liver
  - 150g vs 75g
- Energy calories: chips>chocolate
- Ketone bodies, produced by the liver
- Can't use ketone bodies – liver, heart and brain can
- Insulin increases fructose 2,6 bisphosphate in liver (2<sup>nd</sup> messenger)
- Hormone increases glycolysis in the muscle but not the liver: adrenaline
- Adrenaline
  - Increases blood glucose
  - Prepares muscles
  - Increases blood fatty acids
- Glucose 6-phosphate
  - Affects liver's ability to replace blood glucose using glycogen reserve
  - Fructose 1-6 bisphosphate only affects gluconeogenesis
- Compartments in the liver: cytosol, mitochondria
  - Metabolites – glucose, glycogen, pyruvate, acetyl coA, fatty acyl CoA
  - Transport systems: GLUT, Carnitine transporters
  - Pathways: Glycolysis, TCA, respiratory chain, beta-oxidation
- NAD<sup>+</sup> is necessary for DNA repair and activating longevity genes
  - Lacked up in NADH with high calorie diet
    - Also increases superoxide produced
    - NADH also interacts with iron producing H<sub>2</sub>O<sub>2</sub>

## Plenary 2: Alcohol

### Ethics

- Non-consequentialism – good intention, do things because you think it's right
- Consequentialism – social judgement based on result
- Libertarianism – based on freedom, people can do what they want
- Autonomy – freedom of action, who deserves autonomy?

### Addiction

- A human response, rather than a biochemical one
  - Dopamine? Endogenous opioids, GABA/glutamate
  - Tolerance, withdrawal
- Problems:
  - Dependence
  - Psychological behavioural disorder

### Aetiology of alcohol abuse/dependency

- Biological
  - Genetic predisposition
  - ALDH – problem in enzyme causes build up of acetaldehyde dehydrogenase resulting in nausea, flush
- Psychological
  - Stress, depression
  - Rare to develop and alcohol problem without a pre-existing problem
    - Direction of causality is important
      - Does depression cause people to drink or does alcohol cause depression/mood problems?
- Social
  - Environmental, peers, culture, race, availability, legal status

### Culture

- Western culture
  - Taught from a young age
  - Europe: Finish kill lovers, French kill livers
    - North – binge, drinking to get drunk
    - South – rarely get drunk, drink a lot: chronic problems
- Aboriginals
  - Used to be not allowed thus culture of drinking lots of alcohol out of sight in a small amount of time
  - EtOH was introduced into their culture quickly – didn't have generations to adjust to drinking
    - High rates of abstinence, higher than average population but those who do drink, drink in huge excess
- Islamic culture
- Jewish – orthodox jews drink lots of alcohol in very small amounts

### Industry

- Much money is involved – large multinational companies
  - 80:20 rule, 20% of people consume 80% of the profit
  - Active campaigns against interests of public health
    - Aim to promote policies and education campaigns that won't work

### Prohibition and history

- Whenever in history we have attempted to ban alcohol, the ban has been ultimately unsuccessful and counter-productive
  - Can work in the context of cultural background
  - Problems:
    - Crime, police corruption
    - Drinking in secret
    - Putting gang figures and illegal trade in the seat of power
  - Regulations work better than a ban
- Spirits are so much stronger – thus the name
  - Gin in London → was once prohibited in London, later a tax was put on (when it was realised that the ban was not working)

### What works?

- Strategies:
  - Minimum legal age
  - Governmental monopoly of retail sales
  - Restrictions on hours or days of sale
  - Restrictions on density of sales outlets
  - Taxes on alcohol
  - Sobriety checks
  - Lower blood alcohol limits
  - Drink driving licence suspension
  - Graduated licensing limits
  - Brief interventions for hazardous drinkers
- What works is generally unpopular and what doesn't work generally popular
  - Industry distorts perspective
- Regulatory mechanisms are more effective than cultural tools
  - Eg. drink-driving laws

### Alcohol in society

- Sponsorship and sports advertising
- Alcohol egomaniacs

### Alcohol in medical practice

- Affects all organ systems
  - Acute and chronic harm to self and others
- Abuse is more common than dependency

### Future policies

- Alcopops
  - Marketed to young people to recruit new drinkers
  - Designed to be palatable and disguise the taste
- Opening hours
- Broad taxable reforms
- Outlet density
- Education campaigns

## Expert tutorial: Biochemistry

### Magnesium in glycolysis

- ATP and ADP bind Mg when unbound thus it is required for enzyme function

### Carnitine transport

- Transports across inner membrane
  - Mitochondria have a double membrane system
    - Outer membrane is atypical in that it allows the intermembranous space to be essentially continuous with the cytosol
      - Allows everything through except large things like enzymes
  - Acyl groups are transferred, not CoA
    - Gets the fatty acid chain from cytoplasm into the mitochondria
  - There are pools of CoA in both the cytoplasm and the mitochondrial matrix
- Acyl vs Acetyl
  - Acyl is the generic name, most commonly used to describe long chains
  - Acetyl is the short name (C<sub>2</sub>)
- Fatty acids → → acetyl CoA using 2ATP (ATP→AMP, giving pyrophosphate)
  - Freely diversible

### Glycerol

- Where does catabolism occur?
  - In the cytoplasm: 2 versions of the same enzyme that converts glycerol-3-phosphate into DHAP
    - One in the cytoplasm uses NADH, mitochondria: FADH<sub>2</sub>
    - Mitochondrial enzyme has its active site on the outside of the membrane and thus both enzyme is effectively used in the cytoplasm

### Purine and pyrimidine synthesis

- De novo synthesis
  - Ribose group is built up by cyclic actions
  - Requires more energy
- Salvage synthesis
  - Attachment of base group to ribose group

### Transamination

- Uses:
  - To make AA
  - Conversion of AA to other AA
  - Movement of ammonium ion
- Ammonium
  - Produced when AA are deaminated, and are transported via glutamine and thus are taken to the kidney for secretion as urea
- Liver function tests measure the activity of transaminases
- Exist in many tissues
  - Glutamate dehydrogenase → unique to the liver
    - Deaminates amino acids to make urea
      - amino acids act as carriers, glutamate is the main, however
- Body can't store nitrogen, breaks down the excess

### GTP

- Used in GNG: pyruvate → oxaloacetate



### Other

- Everything is funnelled to acetyl CoA
- CoQ is a carrier in the respiratory chain leading to complex 3
- What do we need to know?
  - PFK
- PDH – lipoamide arm

### PDH

- PDH regulation
  - Control is complicated and varies tissue to tissue
  - Can be controlled both allosterically and hormonally

### More misc

- Acetyl CoA and malonyl CoA are used for fatty acid synthesis
- Pentose phosphate pathway: produces NADPH and ribose sugars
- Theophylline – prevents the breakdown of cAMP via deactivating phosphodiesterase
- F-6 bisphosphate is an allosteric activator of PFK
  - Synthesis is increased by insulin

### Respiratory chain (electron transport chain) and oxidative phosphorylation

- Electron pairs are parcel being passed down chain
  - NADH and FADH<sub>2</sub> donate electrons to enzyme complexes via reduction and reoxidation
- H<sup>+</sup>: chain pumps H<sup>+</sup> across the membrane
  - A few are related to redox, most are not, for redox, most come from regular pumps (energy from redox reaction causing conformational change)

### ATP transport

- Mitochondria make ATP
  - Cytoplasm break down ATP
- Need to transport ATP out and ADP and Pi in
  - Methods:
    - Swap ATP for ADP
    - Phosphate/H<sup>+</sup> symport (uses H<sup>+</sup>) (IE: 3+1)

### Pyruvate transport

- Into the mitochondria via transporter: H<sup>+</sup> symporter
  - Uptake is thus driven by the respiratory chain

### Uncoupling proteins

- Makes the respiratory chain leaky to protons and thus the respiratory chain proceeds faster and no proton gradient is built up to slow it down
  - Cell uses nutrients it has in an uncontrolled way and synthesis of ATP is very inefficiently
- Thus, cell generates heat instead of ATP
  - Nutrients, etc are broken down and thus we burn fat and lose weight

### Crash dieting

- During starvation major source of glucose is:
  - Liver glycogen (24 hours) → GNG (2-3 days) with breakdown of ketone bodies, sk muscle and fat
- When we return to normal weight, gain adipose tissue instead of muscle

SGS7:

### Plenary issues

- Personal responsibility for drinking
- How drinking changes lives
- What makes people think they have a problem

### 4 reasons why people drink

- Socialisation + social pressure
- Taste
- Relaxation and euphoria
  - EtOH potentiates GABA
    - Frontal cortex: decision making/higher functions
  - Depressant: stimulates depression
- Addiction

### Standard drink

- 1 standard:
  - 285ml middy beer
  - 100ml glass of wine
  - 30ml nip of spirits
- 1.5 standards
  - 425ml schooner of beer
  - 375can/stubby
- Recommended intake
  - 2/day
  - 2 alcohol free days
  - No more than 4 drinks on a single occasion
- High risk drinking can result in dependence and health effects
- There is not amount of alcohol that is safe for everyone
  - Men vs women: water/fat ratio, size

### Plenary true stories: Lonely boy Richard + discussion

- **Part 1**
  - Australian NT:  $\frac{3}{4}$  in jail are indigenous men
  - Richard – alcohol abuse from 14/15 years old on a daily basis
    - Drinking is seen by his community as socially acceptable
  - Community
    - Alcohol was banned, but freely available at the bauxite mine 15 minutes away
    - Police have a system to bring home drinkers safely
  - Alcohol has a profound and pervasive effect on Aboriginal communities
  - Richard – following father's footsteps
- Alcohol problem in an aboriginal community, problems with drinking:
  - Culture of bingeing
  - Boredom, no work, demoralisation
  - Available, cheap, legal
  - Money to spend → not much else to spend on
  - Poverty, poor housing
  - "White" right, Dispossession, Addiction
- More alcohol non-drinkers than non-drinkers, but drinkers are heavier than non-indigenous drinkers
- Children and alcohol
  - EtOH available and unmonitored
  - Peer pressure, social environment
  - Truancy – school not seen as important
  - Family alcohol problems and violence at home
- Indigenous population pyramid – looks like a developing country
  - High birth rate, and reduced life expectancy/access to healthcare

- **Part 2**
  - Bauxite mine built and accompanying pub
    - Against community will – court law case: failed
  - NT has more pubs/bottle shops per head than the rest of Australia
    - NT people drink more than the average population
- Alcohol dependence
  - 3 or more of:
    - Compulsion to drink, loss of control, tolerance, EtOH takes priority over other responsibilities, withdrawal effects, persistent drinking despite harm
- Problems for the community:
  - Violence, poverty, crime, social breakdown, suicide, mental health
- Community action
  - Alcohol free community, court case
  - Living away from alcohol supply
- **Part 3**
  - Drinking hurts family
    - Eldest son died from drinking related violence
- Effects of alcohol on the individual – decision making, inhibition, social separation
- Interventions – individuals
  - Brief interventions and motivational interviewing (benefit/disadvantage comparison etc )– to change thinking
  - Hard to stop addiction
    - Alternatives → moderation drinking, other drinks
  - Opportunistic intervention for the risky drinker
    - Intensive intervention for the dependent drinker
- Aim is to help alcoholic recognise and acknowledge that there is a problem and then encourage and support them
  - Anyone can carry out intervention
- Grog book → education
- **Part 4**
  - Richard taken home, fighting in back of car
    - Families left to cope with violence
    - Family breakdown, community not dry
  - Police try to send drinking children home
  - School
    - Truancy is a problem → lose teachers if not enough children come to school
    - Community has to work together
  - Ceremonies/rituals
    - Used to teach law/culture
    - Run by elders and teach discipline to youngsters
  - Laws have been lost because of alcohol
  - Richard begins to take responsibility for action
- **Part 5**
  - Sexual assault
  - Drinking daily for 2 years → left home and lived in the “long grass” near the pub
  - Nami took other son away to old homelands away from grog and temptation

~~~~~ unfinished ~~~~~

## Hospital 2

### Gastrointestinal exam

- Hands:
  - Clubbing, palmar crease pallor, palmar erythema (estrogen)
  - Leukonychia (low albumin)
- Vitals:
  - BP, pulse, etc
- Face:
  - Conjunctival pallor
  - Glossitis (smooth tongue: iron deficiency)
  - Central cyanosis
- Chest:
  - Spider nevi (estrogen in blood)
- ABDOMINAL EXAM  
~~~~~  
~~~~~  
~~~~~
- Inguinal hernia + cough
- Pitting oedema on legs
- Extra:
  - Ask for urine analysis and per rectal exam'

Angular cheilitis/angular stomatitis – inflammatory lesion at corner of mouth (labial commissure)

Unknown aetiology, linked with nutritional deficiencies like vitamin B2 (riboflavin), iron deficiency anaemia, zinc deficiency

Causes: celiac disease, malnutrition

Gynecomastia – development of abnormally large mammary glands in males

Aetiology: imbalance of sex hormones

Cause: excessive adipose tissue, abnormal liver function

\*\*add after hospital 3\*\*

### Urinary symptoms

- Urinary tract infection:
  - Increased frequency
  - Dysuria
  - Fever
  - Pyuria
  - Hematuria
  - Suprapubic abdominal pain
- Stones
  - Abdominal flank pain → loin to groin
    - Sharp, severe, true colicky
  - Hematuria – microscopic (dipstick) and macroscopic
- Prostatic disease – benign prostatic hypertrophy (PBH), prostate cancer
  - LUTS – lower urinary tract symptoms
    - Poor stream
    - Incomplete emptying (urgency)
    - Nocturia
    - Retention → Oligouria (>400ml)/anuria(<100ml)
- Incontinence
  - Stress incontinence or urge incontinence

**\*\*SEE TUTORIAL NOTES\*\***

Problem 1

**A**

Dietary glucose → glucose in gut → glucose in the blood → liver (cytosol) → pyruvate (cytosol) → mitochondria  
→ acetylcoA → citrate (mitochondria) → citrate (cytosol) → acetylcoA (cytosol)  
→ fatty acid (cytosol of liver cells) + glycerol (from glucose) → TAG (liver cell) → TAG (blood: lipoprotein)  
→ VLDL (surface of adipose tissue) → FA (adipose cell) + glycerol (adipose cell) → TAG (adipose cell)

**B**

Skeletal muscle protein → hydrolysis of muscle protein → amino acids (sk muscle) → blood  
→ amino acids (liver: not all are gluconeogenic, good ones are: alanine, aspartate, glutamate)  
→ ketoacids (and amino group → urea in urea cycle)  
→ intermediates in the TCA cycle or gluconeogenesis (eg. pyruvate, oxaloacetate, alpha-ketoglutarate respectively as above)  
→ gluconeogenesis in liver cytoplasm (GNG activated by low insulin, high glucagon and high f 1-6-bisphosphatase)  
→ liver glucose → brain glucose → acetylcoA in neuronal cell (via glycolysis)

**C**

Hydrolysis of TAG in adipose by hormone-sensitive lipase (activated via protein kinase A via phosphorylation in response to glucagon)  
→ adipose tissue fatty acid → liver fatty acid (via blood, bound to albumin)  
→ fatty acyl coA (cytoplasm) → carnitine transport → fatty acyl coA (mitochondria)  
→ acetyl coA (beta oxidation) → ketone bodies (mitochondria) → brain (via blood)  
→ acetyl coA (in mitochondria of neuronal cells)

Problem 2

Stress/fasting state → increased glucagon → activates hormone sensitive G protein  
→ increased activity of adenylate cyclase → increased cAMP → increased protein kinase A activity →  
→ phosphorylation of HMGCoA reductase → decreased cholesterol synthesis to conserve energy (anabolic process)

Note:

- Protein kinase is an allosteric enzyme that phosphorylates several specific enzymes/proteins
  - Phosphorylation activates/deactivates proteins
- In a fast state, low glucose (a stressful physiological situation)
  - Thus, decreased cholesterol synthesis to conserve energy
- Allosteric protein kinase A enzyme
  - Stimulated by ATP, substrate
  - Inhibited by AMP, ADP product

Problem 3

Fatty acids can't be converted into precursor for GNG because acetyl CoA can't be converted into pyruvate  
Even via oxaloacetate – there is no gain since carbons are lost as CO<sub>2</sub> at other end of TCA cycle

Problem 4

- 1kg of stored fat lasts for 5 days, 1kg stored glycogen (2/3 water) lasts for 18 hours (amount stored in liver)
  - 10kg will last 50 days
    - → Starvation diet, only lose 10kg in a month of not eating: takes a long time to lose weight on a starvation diet
  - In a medically supervised starvation diet, the longest time without eating is 8 months (~250 days)

## SGS 8:

### Video: catalyst program

- Pleasure → addiction are related to the reward pathways
  - Food, sleep activate these
  - Drugs/chemicals can hijack the pathway → the system readjusts so that it is hard to live without drugs
- Nature vs nurture
  - Twin studies
  - Smoking is 70% genetic?
- Alcohols:
  - A1/A1 gene – highest risk category for alcoholic etc addiction
    - Get a supercharged high and thus are predisposed to addiction
  - Drug under development → only works on A1/A1 genotype
    - Gives a platform to build psychological etc skills and to prevent addiction

### Article: drug dependence as a chronic medical illness

- Article summary:
  - Analogy comparing drug dependence to a chronic illnesses: hypertension, asthma T2DM to show that it too needs to be considered as a chronic illness in terms of treatment
- Main conclusions:
  - Drug dependence is a social and health problem but a chronic illness rather than an acute illness
  - It is important to treat patients on this basis and to use this approach
- Evidence:
  - Literature review, comparative analysis
    - Looking at: diagnosis, heritability, aetiology and pathophysiology
    - + treatment
- Why do doctors fail to diagnose alcohol problems:
  - Doctors don't ask about alcohol related issues – time constraints
  - Patients don't reveal true intake/habits
  - Doctors are afraid of offending patients
  - Treatments are not thought to be effective
- Why do doctors who diagnose alcohol problems in patients respond inadequately
  - Believe that it is a social, not health problem
  - Some doctors don't know motivational interviewing
  - Doctors believe treatments are ineffective
- Evidence that problematic drinking is genetically mediated
  - ALDH
  - Risk of addiction is similar to chronic diseases based on genetics
  - More studies needed
- Evidence for problematic drinking mediated by psychological factors
  - Dopamine – prevents dopamine reuptake and increases release (euphoria)
    - Causes people to ignore need for drink, food or rest
  - Dopamine response is reactivated by other factors such as seeing the bar, or your drinking partner
- Social factors:
  - Peer pressure, ease of purchase, relapse, dependency
  - Increased problem drinking related to low SES – decreased support, decreased finances, decreased access (knowledge, geography), culture, depression
- Treatment effectiveness and compliance
  - Screening and brief interventions influenced motivation
  - Compliance rates were similar across the board – but not that high
- Summary:
  - Alcohol should be treated as a chronic disease
    - Factors
      - No defined test for alcohol dependence – accurate diagnosis?
      - Genetics – takes responsibility away from patient
      - Psychosocial (vs skin cancer) – still responsible for decisions
    - Treatment – can be effective

## Expert tutorials

- Anatomy
  - Page 71: prac guide
  - Spleen – functions:
    - Immune system – matures WBCs
    - Disposal of RBCs
    - Stores a few 100ml of blood
      - Rupture → blood loss
- Endocrine
  - Type 2 DM: insulin resistance
    - 1 insulin causes 2 GLUT transporters
    - Resistance: 1 insulin causes 1 GLUT transporter, thus go into hyperinsulinaemia – 2x insulin to get same effect
  - Pancreatic transplant
    - Need to give immunosuppressants which causes worse resistance
    - Original pancreas is not removed, the exocrine part is attached to the bladder to drain
  - Complications of DM:
    - Retinopathy – haemorrhages and infarcts
      - Ischaemia leads to release of VEGF – causes vessels to grow all over the place and this increases the risk of haemorrhage
  - Diabetic diet → decreased simple sugars, increased complex carbs
- Nutrition
  - Best way to lose weight → decrease calories, increased energy
    - Keep proportions of food, stick to NHMRC guidelines
  - Increased vitamin C can cause kidney stones
    - If too much vitamin C while pregnant, baby can become accustomed to high vitamin C environment, thus leading to scurvy postnatally
  - Caffeine – excess can lead to arrhythmias, palpitations
    - No more than 5/day

## *Viral hepatitis tutorial*

### Case:

- 34 year old male
  - Presents with:
    - Tiredness for last few weeks
    - Dark urine, nausea, anorexia
    - Abdominal discomfort on the right side
  - Just returned from trekking Nepal
  - History of IV drug use
- Examination
  - Jaundice – yellow sclera
  - Tender upper right quadrant

### Liver function tests

- Normally test (normal ranges)
  - ALT (5-30)
    - An enzyme only produced in the liver
  - Bilirubin (direct and indirect) (direct: 0-0.03, indirect: 0.3-1.9)
- Other tests:
  - AST (10-40)
  - ALP (25-115)
- Case results:
  - Extremely high AST, ALT, Bilirubin
- Conclusions from test results:
  - Liver damage
    - ALT elevated
      - Expect ~1000 in viral hepatitis, can go up to 2000
      - Higher in hepatitis B than hepatitis C
    - These levels would only be raised in the acute phase of disease where there is immune damage
      - In chronic disease – levels return down with recurrent flare-ups

### Diagnoses

- Viral hepatitis
  - Travel – Hepatitis A and E
  - IDU – Hepatitis C, B, D
    - Hepatitis C is less likely because it is often asymptomatic in the acute phase (30% symptomatic)
  - Other – CMV, EBV
- Specimens and tests
  - Hepatitis B
    - Serum, requesting EIA
      - Anti-HBcAg
        - IgM – present infection
        - IgG – chronic/past infection
      - Anti-HBeAg
        - Made with the core, excreted during replication
          - Sign of live infreplication
        - +ve to the E-antigen means there is a bigger immune response and consequently more liver damage
      - Antigen directly
    - HBsAg, AB to HBsAG
  - Hepatitis C
    - IgG found if past infection
    - RNA – via sera PCR if current infection
  - Hepatitis E
    - IgM – detectable, don't go chronic



## Test results

- HBsAg negative, Anti-HBs positive, Anti-HB core IgM and IgG negative, HBeAg negative
- EIA for HEV IgM negative
- EIA for HAV IgM negative
- EIA for HCV antibodies positive
- CMV IgG positive, IgM negative (IgG positive in 50% of adults)
- EBV IgG positive, IgM negative
- Interpretation:
  - HBV in window period or HCV
- Other tests to request to confirm:
  - Repeat EIA to check
  - PCR for HCV DNA – only tells you about present infection
    - Qualitative RNA test
  - Hepatitis C:
    - 30% chance will clear infection, 70% go chronic
  - Hepatitis B:
    - Acute disease acquired in adult life: 10% go chronic, 90% clear
      - Neonate – most go chronic
      - Virus is suppressed? Lies dormant? For 20-30 years
    - Coinfection HIV and HBV HCV common
      - More likely to go chronic
      - Treatment is less effective
- Found to have HCV

## Management and treatment

- Hepatitis C
  - Risk factors → alcohol, male, overweight, old
- Vaccinate against hepatitis A and B
- Drugs:
  - Interferon and/or Ribavirin
    - Adverse effects are important → debate whether to treat in acute phase or to wait for it to possibly clear
  - If decide to treat, perform a quantitative RNA to assess viral load every 4 weeks
    - Treat for 24 weeks (may proceed to 48 weeks)
      - Look for a 2 log drop in viral load at 4 weeks
        - If no drop, cancel treatment after 24 weeks (or earlier)
- Genotype patient – types 2,3 good response to therapy
- Other tests/treatment:
  - Liver biopsy – fine needle
  - Liver transplant
    - Higher success with HBV
    - HCV – recurrent infection

## SGS 9:

### Graham Fellowes – rural GP

- Risk factors for medical practitioners in developing impairment to practice:
  - Stress
  - Long hours, workload
  - Emotional factors – depression
  - Relationship factors
- Types of practitioners at risk of substance problems
  - GPs
  - Psychiatrists
  - Rural
  - Small practice
  - Emergency department
  - Dentists
- Other risk factors for substance abuse problems:
  - Depression
  - Decreased work productivity
  - Tiredness
  - Change in personality
  - Tolerance to alcohol
  - Abuse of alcohol
  - Emotional outbursts (irrational)
  - Neglecting responsibilities
- Connection between tolerance and dependence
  - Tolerance leads to dependence – able to drink more, become more dependence
  - Develop in parallel due to a host of other factors (environmental, social)
- Problems colleagues face when someone is using alcohol
  - Increased workload stress
  - Don't want to interfere
  - Conflict – can he be trusted with patients, should he be referred?
  - Intrusion of privacy
  - Conflict of interests – friend/professional relationship
- Residential treatment:
  - Social support
  - Peers
  - Break drinking habits
  - Different environment
  - Counselling
  - Structure
  - Time off
  - Reminds of responsibilities as a doctor

### Kelly Jones – female binge drinker

- Impact of excessive drinking on health:
  - Liver disease, mental health, pancreatitis, CNS disturbances, acute trauma, violence
- Reasons why women are more susceptible
  - Higher fat/water ratio
  - Smaller size
- Predictors for high alcohol consumption in women:
  - Genetics
  - Social class
  - Marital status
  - Stressful life events
  - Rural
- Estimate weekly consumption:
  - 1STD = 10g of alcohol
  - Recall standard drinks
- Motivational interviewing:
  - What is good/bad about drinking/not drinking
  - 5As
  - Understand patient rather than condemn
  - Look at reasons for behaviour and consequences of actions
  - Think of alternate ways of dealing with things
  - Realise that it is a long term disorder – it takes time to change
- Pharmacological and non-pharmacological strategies
  - Acamprosate, naltrexone, disulfiram
  - Drinking diary, hobbies, goals, rewards
  - Review and monitor
  - Group therapy

### Nutritional history

- Reasons for a nutritional history
  - Obesity
  - Diabetes
  - CVD
  - Anaemia – iron deficiency
  - Underweight
  - Coeliac disease – SI affected by gluten 1% of population
  - Lactose intolerance
  - Chronic kidney disease
  - Vitamin/mineral deficiency
  - Elderly, institutions
  - Mental illness
  - Fussy eaters
  - Vegans
  - Sports people
  - Genetics
  - Acute → gastroenteritis
  - Cancer
- History:
  - Go through what person eats for the whole day
    - Takes a long time, but is very thorough
    - Problems with honesty, variance in diet
  - Screening
    - How many times do you eat out/Eat takeaway/junk food each week
    - Fruit and vegetables – fresh vegetables everyday?
    - Regular meals
    - Breakfast?
    - Soft drinks/fruit juice
    - Dairy products
  - Special cases:
    - Pregnancy, breastfeeding?
    - Diabetes
    - Lost weight without trying to
    - Anaemia
    - Osteoporosis
    - Difficulties in shopping/cooking
  - Overweight issues
    - Gaining weight without trying to?
    - More than 10kg since 20s
    - Tried to lose weight/ how many times?
    - Interest in managing weight? – assessment of motivation

### Urine analysis

- Take dipstick from jar
  - Dip in urine
  - Compare to jar
- Look at in particular:
  - Blood, leukocytes, protein, glucose
  - (Nitrites, ketones)
- Reasons to use dipstick (urinalysis):
  - Blood in urine
  - General infection – especially in children
  - Dysuria, frequency
  - Diabetes
  - Kidney disease

*SG 10:*

**Project presentations**

## Pharmacology tutorial

### Major points

- Most drugs are either weak acids or weak bases
- Unionised molecules generally cross cell membranes more easily
  - In kidney: unionised is reabsorbed, ionised is excreted
- The pH of a body site will influence the degree of ionisation of a drug which therefore affects its ability to cross cell membranes
- Degree of ionisation of a drug is predicted by the Henderson-Hasselbach equation

### Acid-base relations

- $K_a$  is the acid dissociation constant
  - $\text{CH}_3\text{COOH} + \text{H}_2\text{O} \leftrightarrow \text{CH}_3\text{COO}^- + \text{H}_3\text{O}^+$ 
    - $K_{\text{eq}} = \frac{[\text{CH}_3\text{COOH}][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{COO}^-][\text{H}_2\text{O}]}$
    - Water is in excess and thus is excluded
      - $K_a = \frac{[\text{CH}_3\text{COOH}][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{COO}^-]}$
  - The higher the  $K_a$ , the stronger the acid
- $\text{pKa} = -\log K_a$ 
  - low pKa – strong acid, higher pKa – weak acid
  - pKa can be higher than 7

### Henderson-Hasselbach equation

- $\text{pH} = \text{pKa} + \log \frac{[\text{base}]}{[\text{acid}]}$ 
  - thus, if  $[\text{base}] = [\text{acid}]$ ,  $\text{pH} = \text{pKa}$ 
    - ie, 50% ionised, 50% unionised

See tutorial sheet for practice etc

Note:

**ACID likes ACIDIC environment and will remain unionised**  
**BASE likes BASIC environment and will remain unionised**

### Warwick

- 61 yo male
  - End stage kidney disease for 4-5 years
  - AD polycystic kidney disease
    - Family Hx or renal diseases

### Video:

- PKD
  - Cysts in kidney that slow down function and eventually lead to failure
  - Can get to 60 before it cause problems
- Symptoms:
  - Back pain
  - Fatigue, afternoon nap normal
    - Often don't tell doctor about symptoms
  - Morning sickness – nausea, vomiting
  - HBP, 100 + age
- Hx
  - Father had disease, die 48
    - Had tests to check genetics, urea polygram diagnosed
  - Treated for BP
  - Grandmother died at 50
- Lifestyle
  - Relationship broke up, didn't want to pass on disease to any children
- Medications
  - Take up 13/day for BP
  - Diuretics, toilet
- Complications
  - Mitral valve deficiency – repaired
  - Kidney specialist predicted dialysis in 10-15 years
    - GP weekly blood test to monitor creatine
- Dialysis
  - Haemodialysis or peritoneal dialysis
    - Peritoneal complications: peritonitis (mitral valve prolapse contraindicate)
    - Haemodialysis → 3x 5 hours sessions
      - Needle/blood phobia
      - Confronting
      - Bruising
- Improvements
  - Sleep, sleep through the night
  - Appetite improves, lose weight (to the point where he could stop meds for BP)
- Other meds:
  - Vitamin tablets to replace those lost
- Machine
  - Reverse osmolar machine to purify water + dialysis machine
  - Automates process

### Kidneys

- Retroperitoneal, quite medial
  - Referred pain to back
- Functions
  - Filtration, water balance, acid excretion, waste products, hormone product ion(eg. erythropoietin)
- $\frac{1}{4}$  CO, (1/4 of 5L/min)
- Urine made by filters (glomeruli) ~300 000 in each kidney
  - Makes primitive urine, 100ml/min
    - Primitive urine is concentrated/reabsorbed 99% (rate is the glomeruli filtration rate)

## PCKD

- Cystic enlargement of kidney from 12cm to 25cm
  - Can occupy much of the peritoneal cavity
- Cysts begin in childhood, in utero
  - Apparent by teenage years
- Cysts can also be in the spleen/liver
- Benign, salt water inside
  - No association to cancer
- 1:400, 5% sporadic, 25% no FHx
  - Many undiagnosed and never know about it

## Transplants

- Often problems, 19 tablets/day 2 to counter other tablets
  - Immunosuppressants etc

## Symptoms

- Early stage – none
- Mechanical – back/flank pain
- Functional – fatigue, vomiting, lethargy – due to a build up of waste products
- Other – UTI, haematuria, polyuria
- 50-75% progress to chronic liver failure
  - Depends on genetic defects, PKD1/2

## Effects

- Intrarenal
  - Cysts
  - Decreased concentrating ability
  - Hypertension
  - Kidney stones
- Extrarenal
  - LV hypertrophy
  - Abdominal hernias (increased abdominal pressure, large kidneys)
  - Liver/spleen/pancreas cysts
  - Mitral valve prolapse
  - Intrarenal aneurysms (berry aneurysms)

## Genes

- Defect: Polycystin-1 (85%), Polycystin-2 (15%)
  - Code for membrane glycoproteins in the renal tubular epithelium, pancreas and biliary ducts
  - Functions:
    - Proteins, 1: cell membrane receptors; 2: ion channel
    - Involved in producing cilia in the lumen thus regulate the growth and function of the cell
- 2% tubules form cysts, often close off from tubule
- 2<sup>nd</sup> hit hypothesis
  - Somatic mutation that occurs during life is important in PCKD development
  - Associated with macrophages and fibroblast that will cause fibrosis and reduce kidney function

## Dialysis

- Artificial (haemo), human (peritoneal)
  - Semi-permeable membrane that removes toxic products and fluid
- Started when person has 5-10% kidney function, hyperkalaemia or high urea
  - Also if: lethargy, oedema, hypertension, encephalopathy, metabolic flaps
- Decreased urine output
- Fistula formed, artery joined to a vein an to allow flow in vein to increase 300ml/min

### End stage kidney disease

- 9000 dialysis patients, 7000 transplants
  - 6500 haemo, 2500 peritoneal
- \$50 000/year to dialyse
- Diabetes is the commonest cause in AUS, USA, NZ and is increasing

### Transplants

- Considerations:
  - HLA matching
  - Blood group
  - Immunosuppression
- Kidney is attached to the iliac artery in the pelvis and the native kidneys left in the body
- Advantages:
  - Better QOL, survival
- Disadvantages
  - Complications
  - Surgery
  - Infection
  - Malignancy
  - Drugs
  - Waiting lists for donation (or donations from families)



**Refer to lecture**

Public health ethics

- *Need to think in terms of community when dealing with the individual*

Organ transplantation

- Kidney, liver, heart lung etc can be transplanted
- Categories of donor
  - Cadaveric
    - Motor vehicle
    - Brain injury
  - Living
    - Related
    - Unrelated
      - Directed
      - Non-directed
- Issues:
  - Coercion
    - Relatives
    - Poor people
  - Informed consent
    - Parents and children
    - Psychological state
  - Who owns bodies
    - Government? Next of kin?
    - A better system – compulsory donation unless you ‘opt out’ → used in Europe, no organ shortage
  - Pain – do donors feel pain?
  - Brain death – whole brain death or just higher cortical functions
    - When are people ‘dead’, when can we take their organs?
  - Organs from other species
    - Animal rights
    - GM pigs
    - Cross-species disease
- The community will always have ethical objections, communitarian ethics asks us to consider what is best for the community as a whole, sometimes before the rights/needs of the individual

## SGS 11:

### Liver physiology

- Bilirubin (unconjugated) travels in the blood bound to albumin, fat soluble
  - Processing by hepatocytes → conjugation
  - Conjugated bilirubin enters bile and gets into the gut, water soluble
    - Processed by bacteria to urobilinogen
    - Urobilinogen is:
      - Reabsorbed through gut and returned to liver to be put again into bile and to the gut
      - Processed by the kidney to give urobilin which gives urine its colour
      - Remains in the gut, processed to stercobilin which gives stools brown colour

### Liver function tests

- Bilirubin – indicates activity of liver cells/condition of bile duct/amount of red blood cell breakdown
- Alkaline phosphatase, gamma-glutamyltransferase – indicate blockage of the bile duct
  - Plasma membrane enzymes that are cleaved with higher biliary output pressure
- AST, ALT – released on necrosis of hepatocytes
- Albumin, total protein – measures of synthetic liver function
  - Reflects liver function over a longer period

### Case 1

- 43 yo female
  - Recurrent central abdominal pain for a few weeks
  - Dark urine, pale stools
  - Jaundice
- LFT: Br, ALP, GGT raised, everything else normal
- Examination: Distal common bile duct dilated and enlarged
- Diagnosis: obstructive jaundice caused by gallstones
  - Dark urine caused by increased conjugated bilirubin in blood
  - Pale stools caused by lack of bilirubin in bile/gut

### Case 2

- 14 yo female
  - Intermittent pain mild, painless jaundice many years
  - Pallor, splenomegaly
- LFT: Br increased, everything else normal
- FBC: mild anaemia, normal blood cells, but fragile + more young RBCs – normochromic, normocytic with spherocytes
  - Serum haptoglobins decreased
    - Protein that binds to unbound haemoglobin and is removed by spleen
    - Thus is decreased in haemolysis as there is increased Hb released into blood
  - Lactate dehydrogenase increased indicating more haemolysis
- Anaemia
  - Increased haem broken down
    - Increased RBC breakdown in the spleen → splenomegaly
- Increased bilirubin
  - Haem processed to bilirubin, more than can be processed by liver
- Diagnoses:
  - Autoimmune, trauma, cancer, genetic

### Case 3

- 26 yo male
  - Malaise, nausea for a week
  - Urine dark, stools pale, jaundice
  - No risk factors for Hepatitis C, B
- Examination: liver palpable
- LFT: increased Br, ALP, GGT, AST, ALT. normal TP, Alb
  - Thus, not a chronic problem → acute liver damage
- HAV IgM raised
- Diagnosis: Hepatitis A infection
  - Dark urine – increased unconjugated bilirubin in liver, diffuses back into blood
  - Pale stools – no bilirubin conjugation, thus none excreted in bile to gut

### Case 4

- Jaundice, dark urine, weight loss, no abdominal pain
- Examination: tumour on the head of the pancreas
- LFT: increased Br, GGT, ALP, rest normal
  - Thus a biliary obstruction issue
- Diagnosis: painless obstructive jaundice of the bile duct by pancreatic tumour

Indicator	Case 1	Case 2	Case 3	Case 4
<b>RBC Breakdown</b>	N	INCREASED	N	N
<b>Hepatocyte function</b>	N	N	DECREASED	N
<b>Unconjugated bilirubin in blood</b>	N	N/INCREASED	INCREASED	N
<b>Intrahepatic biliary flow</b>	N	N	DECREASED	N
<b>Extrahepatic biliary flow</b>	DECREASED	N	DECREASED	DECREASED
<b>Conjugated bilirubin in blood</b>	INCREASED	N/INCREASED	DECREASED	INCREASED

## Pathology tutorial

### Pots

- Fatty change
  - 3-4 kg in size, greasy, yellow
  - Due to chronic alcohol abuse
  - Reversible
  - LFT:
    - AST, ALT slightly elevated
    - GGT, ALP elevated
  - Complications
    - Can exacerbate a cardiac arrhythmia leading to death
- Alcoholic hepatitis
  - Damage to liver cells → may result in death
  - Accumulation of neutrophils
- Cirrhosis
  - Micronodular
    - Fibrous scar tissue separating regenerating nodules
      - Disruption of lobular architecture
      - Diffuse
    - Often due to alcohol abuse
  - Macronodular
    - Often due to chronic hepatitis B/C
    - Broader fibrous septa formation, thus macronodules
- Hepatocellular carcinoma – on a background of micronodular cirrhosis
  - Often alcoholic base
    - Possibly hep B, C, hemochromatosis
  - Satellite lesions present
  - Primary vs secondary tumour
    - Primary often irregular/larger, secondary metastases – rounded, smaller

### Complications of cirrhosis

- Liver failure
  - Decreased albumin – chronic liver disease
  - Encephalopathy, asterix, confused, coma
    - Waste products from protein metabolism not processed
  - PV hypertension
    - Splenomegaly – dragging sensation on left
      - Hypersplenism
      - May lead to haemolytic anaemia (similar with WBCs and platelets)
    - P-S anastomoses
      - Varices:
        - Haematemesis (submucosal oesophageal veins) – needs transfusion
        - Haemorrhoids
        - Caput medusae
      - Blood bypasses liver, thus is not detoxified
  - Clotting problems
    - Coagulopathy
    - Haemostasis disabled, spleen breaking down platelets
  - Swallowing of blood (from haematemesis)
    - Protein, increase nitrogenous waste

### Alcoholics

- Haematemesis
  - Mallory-weiss tear
  - Peptic ulcers – possibly life threatening
  - Acute erosive gastritis – superficial BVs affected

### Clinical manifestations/signs of liver failure

- Jaundice
- Palmar erythema – due to excess estrogen
- Spider naevi – due to excess estrogen
- Gynecomastia– due to excess estrogen
- Testicular atrophy – due to excess estrogen
- Loss of body hair, loss of libido – due to excess estrogen

### Causes of cirrhosis

- Chronic hepatitis
- Alcohol
- Hemochromatosis
- PBC – primary biliary cirrhosis (autoimmune)
- Secondary biliary cirrhosis
  - Chronic obstruction to the common bile duct
- Cryptogenic cirrhosis

### Hepatitis – viral

- A: Faecal-oral, acute, can sometimes go fulminant
  - PM – massive hepatic necrosis, liver smaller
    - Death from hepatic encephalopathy
  - AST, ALT increased, jaundice
- B, C: parenteral – risk chronic hepatitis → cirrhosis → HCC
- E: 3<sup>rd</sup> trimester of pregnancy, 20% mortality

## Hospital tutorial 3

### Feeling the border of the liver

- May feel:
  - Smooth
  - Round
  - Nodular

### Hernias

- Get the patient to stand up

### Masses

- Characterise the:
  - Site
  - Size
  - Shape
  - Consistency
  - Movability
  - Relations

### Auscultation

- Fluid thrills
  - Liver:
    - Eg: A-V malformation
  - Spleen

### Per-rectal examination

- Tone of anus
  - Get patient to contract
- Feel the cervix
- Masses, 'volcanoes'
- Blood on removal
  - Fresh blood
  - Melena

### Appendicitis

- Rovsing's sign
  - Push on left side, hurts on right
- Psoas
  - Stretch psoas muscle (pull leg back), pain because appendix sits on the psoas muscle

### Peritonism

- Push down, and release suddenly
- Look for:
  - Rigidity
  - Guarding
  - Rebound tenderness
  - Absent bowel sounds

### Ethical issues in article

- Complementary medicine
  - TGA listing vs approval
    - Herbal remedies don't have strict test
      - Can 'put into food' and thus don't need approval
    - No standards on preparation, storage, labels etc
  - Costs \$1 billion to put a drug on the market

### Role-play

- Background:
  - Belgium doctors prescribed a Chinese herbal remedy for slimming to some women
    - These women later are complaining of kidney failure
- Client of the slimming clinic
  - Attended slimming clinic and took drug prescribed by doctors
  - Worried about kidney failure/death
    - Tiredness/fatigue – will this last
  - Options for a transplant? Maybe need a new liver in 6 months
  - Responsibilities
    - To take drugs unchanged, to follow doctor's regimen
- Doctors at the clinic
  - Found drug in Chinese literature, ordered from pharmacist
    - Drug found to be effective in some cases
  - One doctor had more patients with CKD than other – unknown cause, possibly the way his patients were taking the drug/interactions
  - Responsibilities
    - To patients, to recommend a good treatment option
- Dispensing pharmacist
  - Didn't know about drug, trusted doctors
    - Located a supplier in china
    - Arrangements had worked well in the past, used supplier to source drug
  - Relies on supplier for quality control
    - Doesn't have money or time to check all drugs
  - Implicated as at fault by Belgian law – pharmacist is responsible for the quality of drugs they dispense
  - Responsibilities
    - To ensure quality control
    - To ensure quality of the supplier
- Chinese manufacturer
  - Small business in China, employs local workers to pick herbs
    - Contacted by Belgian company and picked local herbs to demand
  - Confident in pickers
    - Standards of pickers?
  - Responsibilities
    - To supply the right herbs and of a standard quality
- Chinese herb-pickers
  - Pick herbs for manufacturers
    - Normally used summer herb, knew that winter herb was not as effective, still picked because manufacturer still paid
  - Responsibilities
    - To supply the right herb with a standard quality to the manufacturers
- Professors of medicine
  - Investigate case

## Swiss cheese model

- Medical error is significant
  - 16.6% of people in hospital have an AE due to iatrogenic causes
- Problems with the system:
  - Health system prevents honesty
  - Blame and shame culture
    - Human error/individuals are found to be at fault
- Prevention
  - Mistakes occur due to human errors/system failure
    - **Active failure** → unsafe acts (eg. dose, wrong test, amputating wrong limb)
    - **Latent conditions** → “latent pathogens” in system (eg. similar labels, bad policies for same name patients)
  - Types of errors
    - Diagnostic, treatment, preventative, miscellaneous
  - Prevention needs to focus on both these, in particular latent conditions
- Reason Swiss cheese model
  - Cheese layers are the defensive layers in the system
    - Holes are the problems in the system (active/latent)
    - Cheese layers shift and when holes line up, accident trajectories occur → **errors**
  - Prevention:
    - Killing the mosquitos (active failure), is not very effective
      - Better to drain the swamp of latent conditions where the mosquitos breed
    - Thus, we should alter the system to minimise/prevent errors due to human failings
      - Eg:
        - Healthcare quality
        - Education
        - Change culture of shame/blame

## Alternative therapies

- Problems
  - Drug interaction
  - Physiological side effects
- Complimentary and alternative medicines (CAMs)
  - Alternative medicines – an approach to health and medicine considered outside conventional medicine
    - Replaces conventional medicine
  - Complimentary medicines are similar to alternative medicines but aim to aid rather than replace conventional medicines
- Complementary medicines:
  - Can be over the counter or herbalist/naturopath prescribed
  - Categories:
    - Herbs, traditional medicines, vitamins/minerals, nutritional supplements, homeopathic medicines
    - Homeopathy – like cure likes, dilution makes things stronger
- Australia
  - Conventional medicine is regulated by the TGA
    - Manufacturing, efficacy, safety, post-market surveillance, advertising, terminology
  - TGA listed (herbs etc)
    - Good manufacturing standards
      - Doesn't tell us all the active ingredients (often unknown), AE, interactions
      - Very little surveillance/monitoring
- Evidence-based medicine on CAMs:
  - Need to consider:
    - Manufacturing
    - Efficacy in preventing disease progression (otherwise, may delay conventional treatments until too late)
    - Complement/drug interference
    - SE vs efficacy/outcome balance
- **Advocacy and anecdote do not = efficacy, there is a 30% placebo effect**



## *Expert tutorials: physiology*

### Colloid osmotic pressure

- Pressure due to protein
  - Only effective osmoles (proteins that don't permeate the capillaries)
  - Attract cations (because proteins have a negative charge often)

### Countercurrent mechanism

- Active countercurrent multiplication
  - Sets up medullary interstitial gradient
    - Occurs in the thick ascending limb of the LH in the outer medulla
  - One side of loop is permeable to water and thus osmolality equalises with interstitium
    - Other side of loop has pumps that can pump to a difference of 200 mOsm
  - Thus, as fluid flows through loops of Henle, gradient is set up
- Passive countercurrent multiplication – urea recycling
  - Needs active to function
    - Occurs in the deeper medulla in the thin ascending loop of Henle, thus only occurs in juxtamedullary nephrons
  - Urea diffuses into tubule following concentration gradient, and takes water with it, this further dilutes the fluid in the tubule increasing the passive diffusion of NaCl following its concentration gradient out into the interstitium
    - More NaCl diffuses out than urea is taken in, thus there is a net increase in interstitium osmolality
  - Urea is returned to interstitium by diffusing out of the collecting duct in the presence of ADH
    - This occurs after becoming more concentrated than interstitium through loss of water through the collecting ductule
- Countercurrent exchange
  - Capillaries in the medulla deliver blood in such a way that osmolar gradient is retained and blood doesn't remove an osmolar imbalance
  - Based on capillary loops that dip through concentration gradient

### Transcellular and paracellular

- Local gradients are important

## SGS 13:

### Glucose and ketones

- Glucose
  - Normally low, or not detected
    - Increased glucose causes dipstick to get darker in colour
  - False +ves/-ves
    - Ketone bodies, acidosis – false –ves
  - Mechanism
    - Glucose oxidase forms gluconic acid and hydrogen peroxidase
    - Moisture, heat can denature proteins and give false –ves
- Ketone bodies
  - Normally none
    - Ketoacidosis or abnormal carbohydrate, lipid digestion +ve
  - Detects acetic acid (not acetone or beta hydroxybutyric acid)
    - Indicator patch changes from buff pink to maroon
  - False +ves: pigmented urine (concentrated); levodopa treatment

### Specific gravity and pH

- Specific gravity
  - Osmolality of solution based on Fe concentration, and refractive index
    - Normal range: 1.001-1.035
      - >1.023 is normal kidney function
  - False readings:
    - Fe concentration only measured, non-iron can cause misreadings
    - Highly buffered alkaline urine can give low readings
    - Increased protein can give high readings
- pH
  - colour change
  - normal values: 4.6-8
    - metabolic acidosis alkalosis
  - Bacterial growth can cause alkaline/acidic urine

### Blood

- Based on peroxide-like activity of Hb
  - Changes colour from orange to green/blue
    - Green spots – intact RBCs, free Hb: entire green
- Want no Hb, a small amount is sufficient to warrant further investigation
  - May indicate urological, nephrological and bleeding disorders
- Limitations
  - Microbial peroxidase, captoten, hypochlorite

### Protein

- Want <150mg/day, >500mg/day is a proteinuria
- False +ves:
  - Tubular overflow
  - Infection, bacterial proteins
  - Temperature elevated, dehydration, UTI, exercise, fever
- Not specific to a particular protein
- Protein-of-error indicators
  - Green – protein, yellow negative

## Nitrites and leukocytes

- Leukocytes:
  - Pyuria, can indicate kidney disease/ UTI
    - Expect WBCs if signs of infection
  - False results:
    - Contamination (false +ve)
    - False –ves: elevated glucose, cephalexin, oxalic acid, tetracycline
  - Based on esterases from granulocytes that catalyse hydrolysis of pigments
- Nitrites
  - Waste product of enteric gram –ve bacteria
  - Normally –ve, more concentration in infection
    - Increases with time I bladder
  - False negative – short incubation in bladder

## Cases

Case	Glucose	Bilirubin	Ketones	SG	Blood	pH	Protein	Nitrites	Leukocytes
1	++			1.010		7	+		
2				1.020	+ (RBC)	7	+		
3	+++		+++	1.015		5			
4	++			1.020		7	++++		

Case	Pathogenesis/clinical presentation	Diagnosis
1	-Renal tubular impairment -lethargy, nausea, nocturia -Hypertensive, pale -Ballotable kidneys	PKD
2	-haematuria, ureteric colic -loin to groin pain	Renal calculi
3	-ketoacidosis - glucosuria -drowsiness, thirst, polyuria	Type 1 diabetes, undiagnosed
4	-proteinuria, glucosuria, hypertension -pitting oedema	Diabetes leading to nephropathy: kidney failure

### Expert tutorial feedback

- Histology
  - Pancreas – look at endocrine and exocrine
    - Endocrine – islets of langerhan's and cells within
    - Exocrine – ducts have cuboidal epithelium
  - Liver
    - Dual blood supply, Sinusoidal capillaries, Kupffer cells, Glisson's capsule – collagen
  - GB
    - Absorptive simple columnar epithelium
  - Kidney
    - PCTs – brush border, 2/3 reabsorption occurs here
    - DCTs – bigger lumen
  - Ureter
    - Muscular
    - Transitional epithelium
    - Star-shaped lumen
  - JG apparatus
    - Located at the side of the glomerulus
    - Mesangial cells in the walls of the glomeruli capillaries
- Pharmacology
  - Treatment of obesity
    - Sibutramine – controls appetite by reducing NA, 5HT reuptake
      - Used BMI>30, reduces BW by 5.9%
      - AE: HBP, headache, insomnia
    - Phentermine – controls appetite by reducing NA reuptake
    - Combination therapy can be useful
      - Increases risk of AE, however
  - Alcohol potentiates GABA
    - GABA vs glutamate
      - Chronic alcoholics have up-regulation of NMDA receptors, which cause imbalance and increased glutamate activity → tremors, anxiety etc
        - Thus, acamprosate inhibits glutamate and lessens withdrawal symptoms
  - St John's Wort can affect normal drugs
  - Overdose of IV drugs easily – clinical error is high
  - 7 factors in drug metabolism
- Biochemistry
  - $\text{NAD}^+ + \text{H}^+ \rightarrow \text{NADH}$ , reduction: not only is a  $\text{H}^+$  gained, also 2  $\text{e}^-$  gained

### Quiz

- SE Asians BMI 23-30 OW
- Leptin targets arcuate nucleus
- Weight loss decreases leptin
- Diabetes → ketones → diabetic ketoacidosis
- Periodic environmental triggers can cause type 1 diabetes
- Glucose 6 phosphatase affects glycogen breakdown as well as GNG
- Married, less likely to be risky drinkers
- Total liver blood flow is 1500 (1000 portal, 500 hepatic), bile 500-1200ml/day produced
- Increased ALP, GGT, bilirubin → choledocholithiasis, gall stones in the common bile duct
- Lesser omentum begins superiorly at porta hepatis, runs in groove of ligamentum venosum to lesser curvature
- Diabetes has increased glucose leading to bacterial growth
- Thick aLH has active pumping of NaCl out of tubule
- Most of renal blood flow goes to the cortex (10% medulla)
- Vasodilation of afferent arterioles causes increased renal blood flow
  - Flow pressure/resistance
- CAMS – TGA listed, not registered