THE ACMA NEWSLETTER

April 2014

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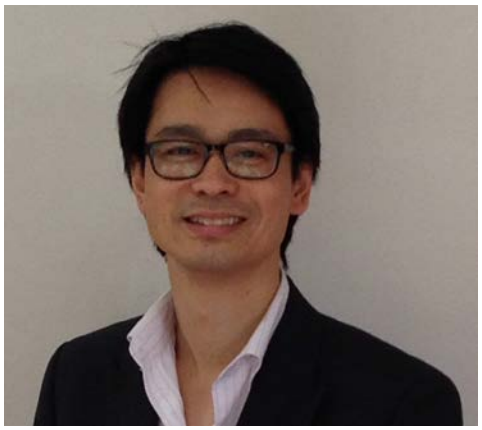
PRESIDENT'S WELCOME



Dear Members,

The first part of the year is now successfully passed. We are now aiming for the conference on 28 June to be held at the Waipuna Conference Centre with an excellent spread of topics and speakers with emphasis on Chinese Health now and in the future. We are advertising far and wide to encourage a greater attendance (Limited 220 places) so I would encourage you to register early as one month out will be the end of the early bird of $100 and will be $150 thereafter.

I have the pleasure of introducing you to the new website which has greater functionality and hopefully with your suggestions we may be able to improve it further.

I have had some great suggestions from some members about what we could do in the future and I would love to accommodate as many of your thoughts as possible. Please continue to let the executive know what your thoughts are.

It has been wonderful to see new members and we would certainly like to encourage more membership and as a result we are looking at how we currently do things and hopefully we will be able to accommodate for as many interested practitioners as possible.

I look forward to your future participation in our upcoming events.

Adrian Wan
ACMA President 2014

THE EDITORS

Hi everyone, it is a great privilege working with ACMA this year. Hope you enjoy reading this newsletter as much as we had fun making it. Let us know if you have any news, pictures, ads or ideas you would like to see in the future newsletters.

You can email us at **editors@acma.org.nz**.

Thank you ☺ -Liz, Maggie, Vicky and Paul

2014 ACMA TEAM

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Vice President
Dr Derek Luo

Past President
Dr Kate Yang

Secretary
Dr Richard Yu

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Dr Carlos Lam

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Alwin Lim

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5th Year – Debra Yeh
4th Year – Vincent Jeong

Student Preclinical Reps
Kenji Kawamura
Harry Yoon
Frank Zhang

Newsletter Editors
Maggie Pan
Elizabeth No
Paul Liao
Vicky Tai

KEY REMINDERS

Membership

We would like to invite existing members to renew their membership through the membership forms available from the ACMA website: http://acma.org.nz/wp-login.php?action=register or through the Membership secretary.

Please go to http://acma.org.nz/membership for more details on payment.

ACMA Website

This year ACMA has launched a new website! Many thanks to Dr Carlos Lam (ACMA webmaster) and Eileen Zhou (YACMA webmaster) for their hard work putting it together.

Visit the website (http://acma.org.nz) to stay in tune about what is happening within our organisation. There will be regular updates on upcoming events such as CMEs, the ACMA Biennial Conference 2014 and social events. Through this website, you can also access current and previous newsletters (which contain CME notes) and view photos from past events.

To make it easier for you to navigate our website, please register on the site. Click the grey ‘Register’ button on the top right corner of the page to do this.

Looking for New Members

Please introduce the Association to your colleagues!

UPCOMING EVENTS

Next CME: May 18th

The next CME meeting will be held on **Sunday 18th of May**, beginning at 5:30pm.

It will be held at **Grand Harbour Chinese Restaurant** (Cnr Pakenham & Customs St West, Viaduct Harbour).

Please RSVP by **Friday 16th of May:** http://bit.ly/2014acmaCME

We look forward to seeing everyone there.

Future CME Dates

14th September (CME) and **9th November** (AGM)

ACMA Conference

ACMA proudly presents its biennial conference:

"To the Future: Chinese Health in New Zealand."

It will be held on the **28th of June** (Saturday) from 8.30am to 4.30pm at the **Waipuna Conference Centre** in Mt Wellington.

Conference will cover four main domains:

Allied Health, Internal Medicine, Surgery and Mental Health.

Early bird registration before May 28th: **$100** (three meals included)
Registration after May 28th: $150

Register online here: **http://acma.org.nz/conference-registration/**

YACMA News

YACMA RECRUITMENT- O WEEK STALL

The stalls day was an opportunity for students to meet the people in YACMA, get to know more about who we are, and what we do. Since no YACMA event is complete without good food, students were treated to Kenji's special fried rice, which disappeared within minutes, establishing Kenji's undisputable reputation as the best fried rice chef around. Also during O week fortune cookies were distributed to the 2nd and 3rd year classes to further promote the society. Making enough fortune cookies to feed the two classes was no small task, and we thank all those who worked tirelessly till midnights to make this happen.

YACMA BBQ

Held at Outhwaite Park on 14th March, this event is traditionally seen as a crucial part of the recruitment process. And this year was no different, with the BBQ drawing crowds of hungry 2nd and 3rd years. We anticipated the huge mob of people, and thanks again must be given to those who helped out! Feedback was extremely positive from those who went, and the laptops were never left idle, thanks to the continuous stream of people who wanted to sign up.

YACMA YUMCHA

One of the most anticipated events on the YACMA calendar, the annual YACMA YUMCHAR was held on 12th April. After a morning of icebreaking games at the domain, we went to the Sichuan Restaurant in Newmarket. Any initial doubts of not having enough food (for so many people!) were quickly dispelled as the yumchar trolleys rolled in and out of the kitchens. The students were all impressed with the huge variety of authentic 'dimsum', and the event served as a most fitting way to start the mid semester holidays.

Special thanks to Martin Lu, Shan Gunaratna, Arkar Thein, Brian Tse, Tae Gon Yoo and all YACMA exec members for events organisation, YACMA members for the memorable times and ACMA and MAS for financial support. ☺

An INTERVIEW with Dr Kristine Ng

Dr Kristine Ng is a Rheumatologist at Waitemata District Health Board. She was born in Malaysia and graduated from the University of New South Wales Medical School at Sydney, Australia in 1994. After working as a junior doctor in Australia for a few years, she moved to New Zealand. She did most of her rheumatology and internal medicine advanced training in Auckland.

She was awarded the Rose Hellaby Medical Scholarship for 2 years that enabled her to undertake post graduate research at University College London (UCL), United Kingdom. She returned to New Zealand in 2009 to take up a Rheumatology consultant position at North Shore and Waitakere Hospitals. She started private practice in 2010 and recently moved her private practice to the North Shore area.

Many students don't understand much about rheumatology. Can you tell us more about this specialty?

Rheumatology is a medical speciality that deals with conditions involving joints, soft tissues and autoimmune disorders. A lot of these conditions are due to problems with the immune system. As a rheumatologist, some of the common conditions I deal with are rheumatoid arthritis, lupus, psoriatic arthritis and gout. Other less common conditions that I treat are scleroderma, ankylosing spondylitis and vasculitis.

What inspired your interest in rheumatology?

I worked as a medical registrar in Waikato Hospital many years ago and one of my rotations involved running the rheumatology clinics. I was fascinated with how a complex, aberrant immune system in susceptible individuals can cause an autoimmune problem. There is still a lot unknown about the immune pathways in our body despite extensive research in this area. Some of this research has translated to the development of new drugs and biologics that are more effective in controlling disease.

What do you like most about it?

Most rheumatology conditions are chronic diseases that require ongoing input from a rheumatologist. I like this aspect as a good patient-doctor relationship is essential in the management of these patients. Dealing with the diagnosis of a chronic arthritis can be difficult especially when it impacts on the patient's ability to work and function in day to day activities. It is most rewarding when their arthritis is treated successfully and they return to their normal lifestyle.

The other aspect I like is that most rheumatology conditions are multisystem disorders. A prime example is lupus which is my area of interest. Lupus commonly affects skin and joints but can also affect any part of the body. It can affect important organs like the brain and kidneys in some patients. Often I co-manage these patients with other specialists and I enjoy that multidisciplinary interaction. I enjoy the challenge of treating these complex conditions as patients may present with a wide variety of symptoms.

When working as a rheumatologist, what does a daily schedule look like?

Every day is different! Most of my work is based on running outpatient clinics. I have a daily

clinic for 3 days in public and one day in private practice. There are other commitments including XR meetings with our musculoskeletal radiologist for discussion of interesting cases. I conduct rheumatology clinical trials and usually see my trial patients once a week in the research clinic at North Shore Hospital.

As an Honorary Senior Clinical Lecturer with the University of Auckland, I teach 3rd year medical students. This aspect is enjoyable because it is the first time the students have clinical contact with 'real life' patients. I teach them how to interview and examine patients. The students are really enthusiastic in learning and it is great to see and nurture this.

I am a medical advisor for the Arthritis New Zealand grants committee. This involves reviewing research grants and summer studentship applications for approval.

What is the most challenging/interesting case you have encountered in rheumatology?

There are many but I can tell you about a recent case. A middle-aged Chinese man came to see me for ill health over the last 6 months. He had weight loss, muscle fatigue and dry mouth. The patient had seen a number of different doctors with no diagnosis so was understandably frustrated. He was referred to consider if he had Sjogren's Syndrome (an autoimmune condition that affects the tear ducts and salivary glands; many patients present with dry mouth and eyes). After a careful history and examination, I thought he may have a primary neurological problem. I referred him to a neurologist who performed further tests, confirming he had a rare autoimmune neurological condition that causes muscle weakness of the limbs. The dry mouth was due to the involvement of the autonomic nervous system. He did not have Sjogren's syndrome after all. This case highlights the importance of getting a thorough history and examination and looking at the 'whole picture'.

Can you please tell us about your research?

One of the research trials explores the use of a new biologic drug that targets the B cells in the treatment of lupus. Another study done in collaboration with respiratory services at Auckland Hospital examines the significance of myositis autoantibodies in idiopathic inflammatory myositis. A third study looks at the pulmonary hypertension screening practices of NZ rheumatologists in patients with scleroderma.

What advice do you have for current medical students?

Try to get as much clinical exposure to different specialities. If you do decide to specialise, there is no rush to finish advanced training. It is invaluable to have the experience of different rotations when you are a junior doctor. This makes you a more experienced and clinically mature physician when you become a consultant. You have many years ahead to be a consultant. I strongly advocate going overseas for your elective or fellowship in the postgraduate years. It is always good to get 'out of the fish bowl' and see how other countries practice medicine. Lastly, if you are female and want to start a family, do not wait till the time is right, as often there is no "right time". Admittedly it is a difficult juggle between family and career especially for women.

What do you enjoy doing in your spare time?

I have very little spare time with work and being mum to my 6 year old son. I enjoy spending time relaxing with my family and being a Malaysian I love my food!

Something about you that may surprise people?

When I was living in London, I had my brush with fame and personally met Dido, the British singer and songwriter. She has an amazing voice and even performed in one of our rheumatology conferences!

What piqued your interest in ACMA?

After living in 3 different continents, I think it's important to retain our Chinese heritage that identifies our roots yet assimilating to live in a western country. Joining the ACMA maintains collegiality with other Chinese health providers. The link of ACMA with YACMA is great as it nurtures and guides our younger generation. I joined the executive as I felt it was my way to contribute to the society.

Thank you Kristine ☺

Restaurant Review #1 by Maggie Pan

Fine Dining: Euro Restaurant and Bar

Renowned as the restaurant created by MasterChef judge Simon Gault, I was drawn to test it out

For $40 mains, I expected much more finesse than a large piece of fish and a few accompanying vegetables. Euro surely uses fresh ingredients and the portions sizes are good but for fine dining the food could have more complexity. Food was slightly on the bland and overcooked side and presentation could be better. But the ambient atmosphere makes up for that, with good views of the harbour and a good sea breeze, definitely a good place to catch up with friends and family. AND if you're an oyster fan, every March there is $19 for a dozen of freshly shucked Bluff oysters!

Our rating 3/5
Price $$$
Food 3/5
Atmosphere 5/5
Service 5/5

Euro Restaurant & Bar
137-147 Quay St
(Shed 22, Princes Wharf)
Hours: Mon-Sun 12pm-Late

Casual Dining: Depot Eatery

I now understand why there was an hour wait for a table, even on a Monday night. (Two and a half on a Friday night! Maybe because they don't take reservations.) A good buzz, a great selection of NZ wines both on tap and in bottles, and most importantly food that stimulates your curiosity yet delivers on taste. The only things that you might complain about are the small portions. If you're sick of the usual steak at the pub, it's time to try something new at Depot from beef cheeks to pork hock. Although not your usual, the combinations of flavours work well to entertain your palate. It's a "sharing plate" type of restaurant, perfect for a date or catch up with a friend where you can order a range of plates to share. And again if you're a fresh seafood enthusiast they do a range of freshly shucked clams and oysters at $2.50 and $5.50 each respectively. A must try is the "Snapper Sliders" they even have one dedicated chef to make these delightful mini-burgers.

Our rating: 5/5
Price $$
Food 5/5
Atmosphere 4/5
Service 3/5

Depot Eatery and Oyster Bar
86 Federal Street
Skycity Complex
Hours: Mon-Sun 7am-Late

Updates in Endocrinology & Diabetes

Presented by Dr. Pui Ling Chan, Endocrinologist

ACMA CME 16.03.2014

Outline of talk – *What's new/important*?

- Thyroid
- PCOS
- Bones
- Diabetes

Thyroid

- Graves' Disease
- Subclinical hyperthyroidism
- Thyroiditis
- Thyroxine/Thyroid extract

Graves' disease

- A form of autoimmune thyroid disease
- Genetic factors account for 80% susceptibility
- Sisters and children of female with GD have a 5-8% risk of developing GD
- Environmental factors
- Excessive thyroid stimulation

Graves' disease: Clinical manifestations:

Symptoms

- Hyperactivity/irritability
- Heat intolerance
- ↑sweating
- Palpitation
- Fatigue, weakness
- Hand tremors
- Loose stool
- Weight loss with ↑appetite
- Oligo or amenorrhoea, loss of libido

Signs

- Sinus tachycardia
- Atrial fibrillation
- Fine hand tremor
- Warm, moist skin
- Hair loss
- Muscle weakness & wasting
- Congestive heart failure
- *Periodic paralysis (Asian)*

Graves' disease : Investigations

- ↑ free T4 and/or T3; ↓ TSH
- Thyroid antibodies – usually ↑↑(esp. Anti-TPO, lesser extent anti-thyroglobulin)
- ***Thyroid Stimulating Immunoglobulins (TSH Receptor Antibody, TRAb) (+) in almost 100% of cases***
- Radionuclide thyroid scan (thyroid scintigraphy-99Technitium pertechnetate): ↑homogenous uptake

Graves' disease: Specific manifestations

- Diffuse goitre
- *Ophthalmopathy*
- Localised dermopathy (pretibial myxoedema)
- Thyroid acropachy (rarest)
- Type 1 DM
- Addison's disease
- Vitiligo
- Coeliac disease
- Myasthenia gravis



Graves' disease: Medical treatment

- Carbimazole : inhibit thyroid hormone synthesis
- Prophylthiouracil : inhibit T4 to T3 conversion
- Beta blockers
- 5mg carbimazole = 50mg PTU
- *Start 20-30mg/day*, monitor every 4-8weeks
- Carbimazole can be given as **single dose**
- Duration 18 months to induce remission
- 30-40% remain euthyroid 10yrs after tx discontinuation
- Adverse effects: GI symptoms, taste/smell alteration, agranulocytosis (0.1-0.5%), rash, urticaria, arthralgia, cholestatic jaundice, elevated ALT/AST, ANCA(+) vasculitis (PTU)

Graves' disease: Radioiodine therapy 131I

- Used since 1940s
- Definitive treatment for multinodular goitre and adenoma
- Relapsed Graves' disease
- Primary goal is to destroy hyperfunctioning thyroid tissue
- Administered orally as a drink (colorless, odorless, tasteless)
- Dose of 400-800MBq sufficient to treat in 90% of cases
- Discontinue ATD 7days before RAI, then re-commenced after tx & withdrawn gradually
- In general 50-70% patients restore normal thyroid function within 6-8 weeks of receiving RAI. Shrinkgae of goitre occurs but is slower
- No excess risk of cancer

More on RAI 131I

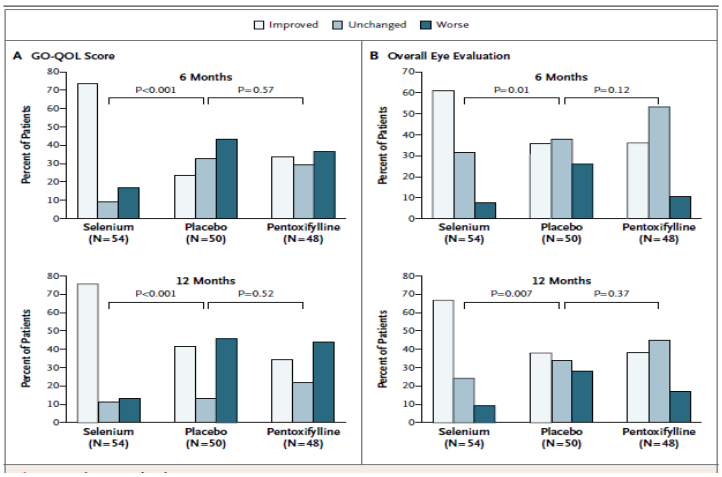
Contraindications

- ➢ Young children
- ➢ Pregnant & lactating female
- ➢ Graves' ophthalmopathy (especially smoker)

Caveats

- ❑ Control of disease may not occur for weeks or months
- ❑ >1 treatment maybe needed (dose-dependent)
- ❑ Use of Iodine-containing compound (e.g. amiodarone)
- ❑ Avoid pregnancy for minimum 6 months following RAI
- ❑ Hypothyroidism 50% at 10 years, continues to increase thereafter

NEJM May 19 2011 : Selenium and the course of mild Grave's Orbipathy



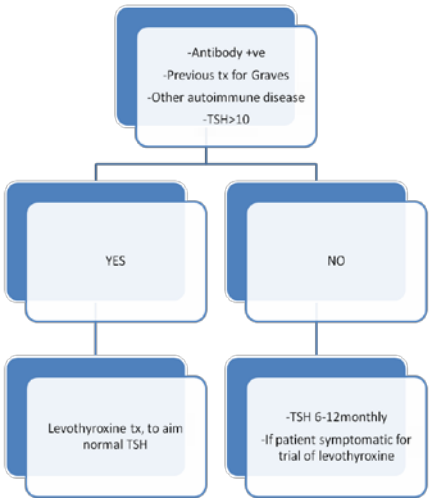
Subclinical hyperthyroidism

- TSH < 0.5 mU/L, Normal T4 & T3
- Subtle symptoms of thyrotoxicosis may be present
- Causes: Graves' disease, toxic nodules, levothyroxine treatment
- The evidence of being risk factor for atrial fibrillation and osteoporosis is definitive
- In older patients with AF or osteoporosis, 131I is best option
- Dose of levothyroxine should be reduced, especially if patient develops:

1. Angina, heart failure, new AF
2. Accelerated bone loss
3. Borderline high serum T3

- In cases of treated thyroid cancer aim TSH 0.1-0.5 mU/mL)

Algorithm for management of subclinical hypothyroidism



Thyroiditis

Causes and characteristics of thyroiditis	
Cause	*Characteristic features*
Hashimoto's (autoimmune) thyroiditis	Usually hypothyroidism, rarely hyperthyroid
Subacute (de Quervain) thyroiditis	Viral in origin Early thyrotoxicosis, occ. late hypothyroidism
Postpartum thyroiditis	Transient hyper- or hypothyroidism
Drug-induced	Amiodarone, Interferon-α, lithium
Riedel thyroiditis	Extensive fibrosis & hardwood consistency of thyroid, usually normal TFTs
Radiation thyroiditis	Transient thyrotoxicosis
Pyogenic thyroiditis	Infection

Hashimoto's (autoimmune) thyroiditis

- Painless goitre
- Normal, subclinical or overt hypothyroidism
- Maybe thyrotoxic with high antithyroid antibodies
- Anti-thyroglobulin (+) in 20-25%
- Anti-TPO (+) in >90%
- Hypothyroidism is easily corrected with levothyroxine
- *Rapidly enlarging goitre should be referred for FNA* (risk of thyroid lymphoma)
- *Painful goitre* could be treated with short course of 40mg Prednisone

Subacute thyroiditis

- Viral in origin
- Sx: Pronounced asthenia, malaise, painful thyroid, fever, thyrotoxicosis
- Characteristic ↑ *ESR*
- Low radionuclide uptake
- Initially hyperthyroid, later hypothyroid (15%)
- Tx: NSAID (mild), Prednisone 20-40mg/d (severe), propranolol
- Tx can be withdrawn when T4 returns to normal
- *Carbimazole or PTU <u>not</u> usually indicated*

Thyroxine (T4)

- Thyroxine (T4) is standard treatment of choice for hypothyroidism, esp. If TSH>10mU/L
- Initial dose 1.6mcg/kg/day, older patient 25-50mcg/day
- Empty stomach.
- Coffee, omeprazole, iron, calcium, H. pylori atrophic gastritis will reduce T4 absorption
- Symptoms resolved within 2-3 weeks
- Re-evaluate TFTs after 6 weeks
- Aim to normalise TSH 0.4-4.0 mU/L

Thyroid extract (desiccated thyroid)

- Porcine or mixed bovine & porcine thyroid glands, dried & powdered for therapeutic use
- All brands contain mixture of T4 and T3 (usually 80% T4 and 20% T3)
- Has become associated with alternative and complementary medicine practitioners
- Has limited quality control and marketed as « bioidentical hormone » by FDA. Purity not monitored, safety not tested in trials, risks unknown, insufficient scientific evidence
- Should **not** be used as thyroid replacement therapy

Polycystic Ovary Syndrome

Main treatment regimen for PCOS

Box 1. Summary of potential targeted treatment options for polycystic ovary syndrome (PCOS)

Oligomenorrhoea/amenorrhoea

- Lifestyle change (5%–10% weight loss + structured exercise)
- Oral contraceptive pill (OCP) (low oestrogen doses [eg, 20 µg] may have less impact on insulin resistance)[47]
- Cyclic progestins (eg, 10 mg medroxyprogesterone acetate 10–14 days every 2–3 months)
- Metformin (improves ovulation and menstrual cyclicity)

Hirsutism

Choice of options depends on patient preferences; impact on wellbeing; and access and affordability:[44]

- Self-administered and professional cosmetic therapy are first line (laser recommended)
- Eflornithine cream can be added and may induce a more rapid response
- If cosmetic therapy is not adequate, pharmacological therapy can be considered
- Pharmacological therapy
  - Medical therapy if patient is concerned and cosmetic therapy is ineffective/ inaccessible/unaffordable
  - Primary therapy is the OCP (monitor glucose tolerance in those at risk of diabetes)
  - Anti-androgen monotherapy (eg, spironolactone or cyproterone acetate) should not be used without adequate contraception
  - Trial therapies for ≥ 6 months before changing dose or medication
  - Combination therapy — If ≥ 6 months of OCP is ineffective, add anti-androgen to OCP (twice daily spironolactone > 50 mg or cyproterone acetate 25 mg/day, days 1–10 of OCP)

Infertility

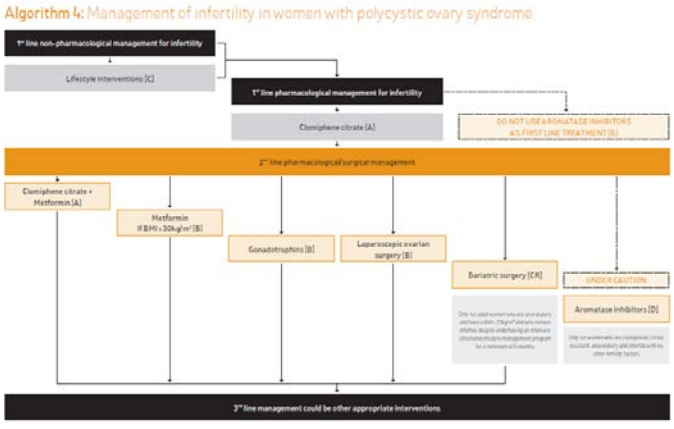
- Lifestyle intervention (to optimise preconception health and fertility and reduce pregnancy and long-term complications)
- Advise on folate, smoking cessation and optimal weight and exercise before conception
- Given age-related infertility, advise women to optimise family initiation
- Infertility therapies may include clomiphene citrate, metformin, gonadotrophins, surgery and in-vitro fertilisation.

Cardiometabolic risk

- Lifestyle change: > 5% weight loss in those who are overweight reduces diabetes risk by approximately 50%–60% in high-risk groups[48]
- Optimise cardiovascular risk factors
- Consider metformin* (reduces the risk of diabetes by ~50% in adherent high-risk groups)[48]

Adapted and reproduced with permission from Teede et al,[9] not generated directly from the evidence-based guidelines. Hirsutism therapy is summarised from existing hirsutism clinical practice guidelines.[4,44] * Metformin and the OCP are not currently approved for use to manage PCOS by many regulatory bodies. The OCP is indicated for contraception and metformin for diabetes. However, their use is supported by evidence and is recommended by international and national specialist societies.[49]

PCOS Australian Alliance



Osteoporosis – What's new?

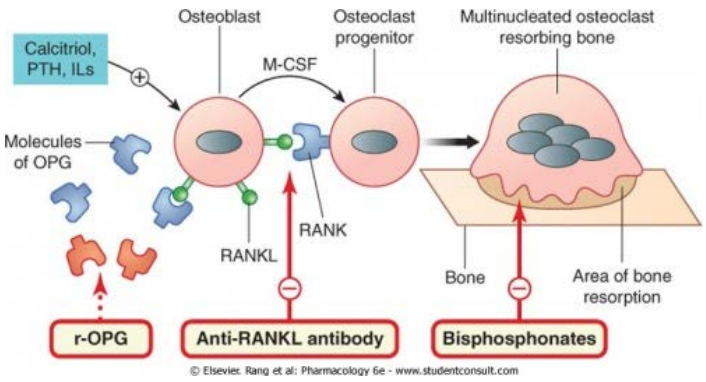
Bisphosphonate and atypical subtrochanteric femoral fracture

- ❑ Safety issue published by FDA in 2010
- ❑ Long-term use (≥5yrs) ↑ risk but absolute risk is **low** (3 to 50 cases per 100,000 person-years)
- ❑ **Drug holiday** after 5yrs of Fosamax – P1NP annually & DXA 2-yearly

Teriparatide (Forteo®)

- ❑ Fully funded in NZ, form SA1139
- ❑ 20µg once daily, subcutaneously
- ❑ Switch on osteoblast
- ❑ Proven to reduce vertebral # by 2/3
- ❑ Maxium lifetime treatment period of 24 months (risk of osteosarcoma)

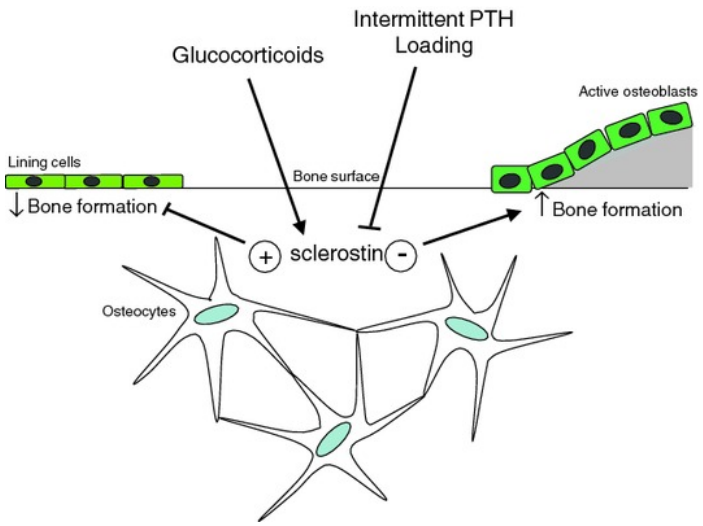
Denusomab



Not currently marketed in NZ

↓ Osteoclast numbers & function

Monoclonal anti-sclerostin antibody

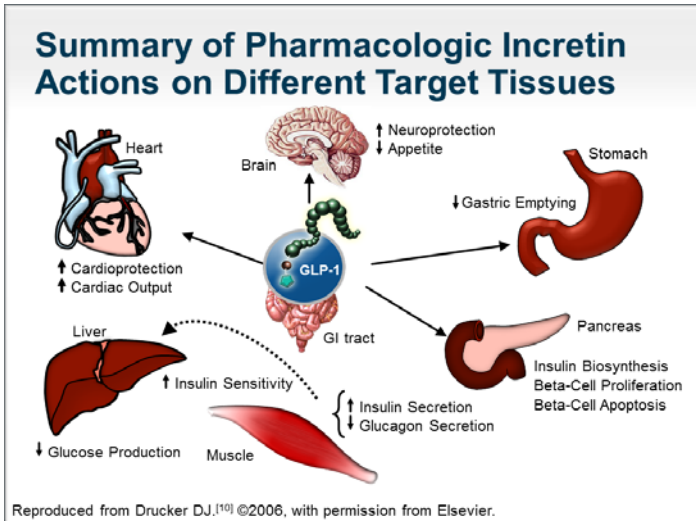


Osteocytes -> Sclerostin -> Anti-osteoblast

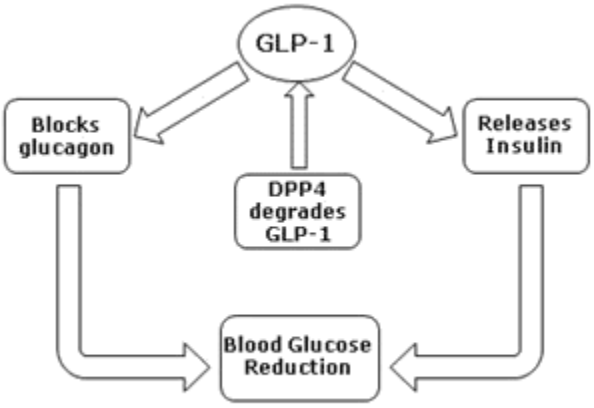
Diabetes – What's new?

- Insulin pump & consumables fully funded by PHARMAC (Sept 2012)
- Insulin Pump, infusion sets, reservoirs
- Diabetes team
- Total daily dose -20%, split 50/50 basal/bolus
- Largest basal rate first thing in morning, lowest overnight

Incretin-based therapy



GLP-1 agonist & DPP4 inhibitors



GLP-1 is involved in blood glucose regulation

GLP: Glucagon-like peptide

DPP4: Dipeptidyl peptidase 4

Pros:

- ➢ Effective tx (add-on to metformin)
- ➢ Weight loss property

Risks:

- ❖ Pancreatitis/Pancreatic cancer with GLP-1 agonists
- ❖ Cardiovascular safety of DPP-4 inhibitors
- ❖ Nausea
- ❖ Cost/availability in NZ

The Thiazolidinediones

PIOGLITAZONE

Pros:

- Efficacy: 1.5% ↓ in HbA1c (monotherapy)
- ↑insulin sensitivity, ↑glucose utilisation
- May improve early β-cell dysfunction
- Minimal hypoglycaemia

Risks:

- ❑ Rosiglitazone-↑MI
- ❑ Pioglitazone (PROactive study) – ↑all-cause mortality, MI & stroke
- ❑ Fluid retention, heart failure
- ❑ Bladder cancer (PIO) – HR 1.22
- ❑ Fracture risk

Current recommendations for Pioglitazone:

- ❑ Not to be used as first line therapy or diabetes prevention
- ❑ Could be considered as an add-on to metformin if insulin or SU contraindicated
- ❑ Weighing risk of heart problem, weight gain or fracture
- ❑ Discuss about risk of bladder cancer

How well do sulfonylureas work?

Estimating the effect of sulfonylurea on HbA_{1c} in diabetes: a systematic review and meta-analysis

Diabetologia (2013) 56:973–984

Meta-analysis of 31 trials:

- SUs by themselves lower HBA1c by 17mmol/mol (which is as good as the newer oral agents).
- SUs added to other oral diabetes drugs lower the HBA1c by 18 mmol/mol.
- SUs added to insulin lower HBA1c by 6 mmol/mol.
- High dose SUs did not lower HBA1c more than low dose.
- SU were associated with more hypoglycaemic episodes but not other adverse events.

Is our trust in Metformin justified?

Effects of Metformin Versus Glipizide on Cardiovascular Outcomes in Patients With Type 2 Diabetes and Coronary Artery Disease

Diabetes Care 36:1304–1311, 2013

- 304 people with T2D and pre-existing CAD were randomised to glipizide or metformin for 3 years
- Follow-up after 5 years
- There was a 46% reduced risk of a cardiovascular event or death in the metformin group.

Sodium Glucose co-transporter (SGLT) inhibitors

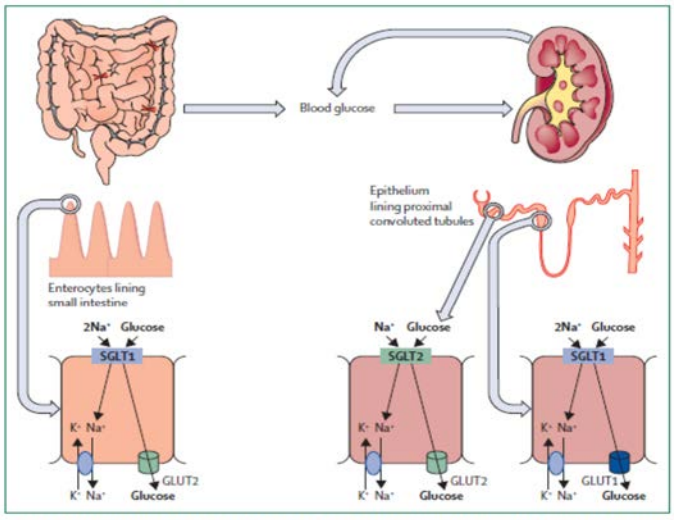


Figure 1: **Sodium glucose cotransporters (SGLT1 and SGLT2) and facilitative glucose transporters (GLUT1 and GLUT2) in the intestine and renal proximal tubules**

SGLT1 is a high-affinity low-capacity transporter and SGLT2 is a low-affinity high-capacity cotransporter. SGLT1 and SGLT2 are secondary active cotransporters, driven by the Na^+/K^+-ATPase pump, which actively extrudes sodium across the basolateral membrane.[4,9,10]

- Dapagifozin, Canaglifozin, Empaglifozin
- Durable glucose-lowering effects
- Assist weight loss
- Could help reduce BP
- Increase risk of UTI
- Might be considered for T1DM…
- Not available in NZ as yet

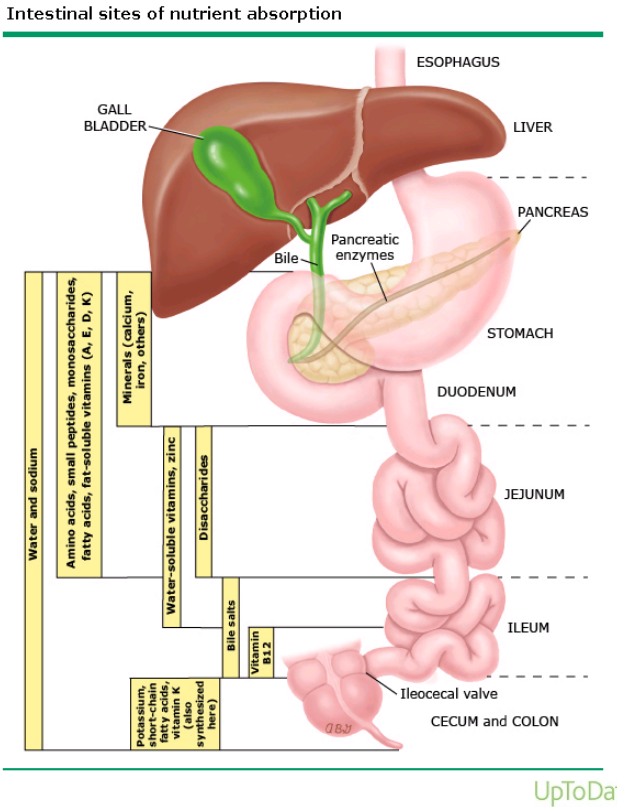
Gastrointestinal Problems after Surgery

Presented by Dr Derek Luo

ACMA CME 16.03.2014

Outline

1. Consequences of bowel resection
2. Post cholecystectomy Syndrome
3. Dumping Syndrome



Short Bowel Syndrome

-Malabsorption following massive small bowel resection

-Macronutrient and Micronutrients

-Most common cause of intestinal failure

-Usually in patients with Crohn's disease, malignancy, radiation, vascular insufficiency

Risks of Short Bowel

-Normal small bowel length 480cm

- <180cm risk of short bowel
- <60cm but with a colon

-Risk factors For SBS

- Length of resection
- Site
- Presence or absence of ICV

Jejunal Resection : Consequences

-Long vili – large absorptive surface

-High concentration of digestive enzymes

-Transport carrier protiens

-Digestive and absorptive site for most nutrients

-Resection results in temporary reduction in absorption

Ileal Resection : Consequences

-Vitamin B12 deficiency – disrupted in >60cm ileum resected

-Bile salt deficiency and fat malabsoprtion – disrupted if >100cm ileum resected

-Fluid absorption – absorbs jejunal fluid – results in fluid and electrolyte losses

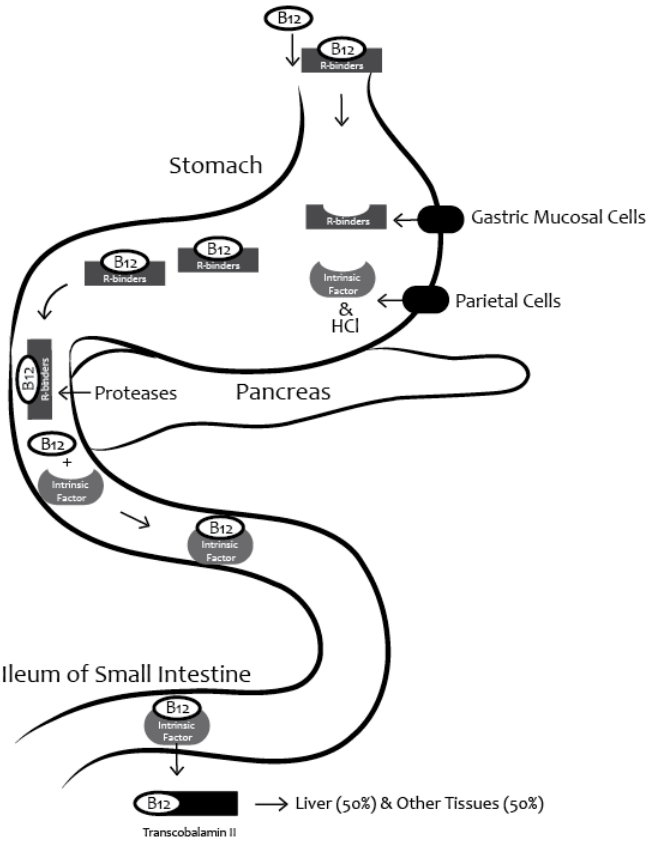
-Compensatory increase by liver

-Fat soluble vitamin deficiency

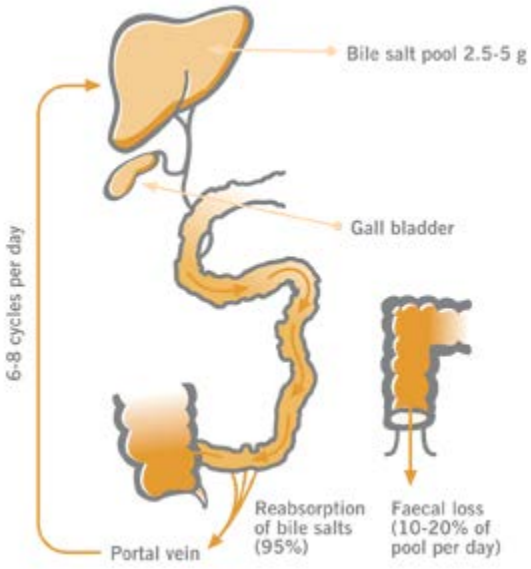
-Excessive absorption of oxalate – kidney stones

-Loss of ileal brake – unabsorbed lipids reach ileum delays gastric emptying (mediated by YY peptide)

Vitamin B12 absorption



Bile acid absorption



Loss of Ileo-caecal valve

-Important barrier to reflux of faeces into small bowel

-Regulates passage of fluid and nutrients from ileum into the colon

-Requires longer parenteral nutrition – harder to wean

-Effects

>Reduction in small bowel transit time – less absorption

>Small bowel bacterial overgrowth – B12/fat and bile salt mal-absorption.

Normal Colonic Function

-Absorption

- Water absorption
- Electrolytes
- Short chain Fatty Acids
- 15% energy requirements – fermented carbohydrates

-Slows transit – stimulates intestinal adaptation

-If have short bowel syndrome but intact colon – able to absorb 50% energy requirements in colon

-Retained colon – adaptation after small bowel resection

Ileal Adapation

-After resection, ileum able to adapt

-Short vili become longer

-Intestinal length can increase

-Diameter bigger

-Motor function

-Upregulation of brush border enzymes and transporters

-Diameter bigger

-Motor function

-Upregulation of brush border enzymes and transporters

Ileal Adaptation : Nutrient effects

-Enteral feeding Best stimulant of intestinal adaptation presence of nutrients

-Mediated by growth factors and biliary and pancreatic secretions

>Arginine – reduces intestinal permeability, enhances adaptation

>Glutamine – reverses intestinal hypoplasia

>Triglycerides – long chain better than medium chain promotes adapatation (but medium chain absorbed better)

>Omega – 3 fatty acids – adaptation of small and large bowel

Ileal adaptation: Gut Hormones

-Glucagon-like peptide 2 (GLP-2) induces adapation after mid-small bowel resection

-Growth Hormones studies with Glutamine – results inconclusive

-Prostaglandins needed – NSAIDs inhibit adaptation

-Gut Hormones also affect

>Motility &Loss of ileal brake

>Hypergastrinaemia – loss of negative feedback – leading to PUD and Oesophagitis (exacerbated by delayed gastric emptying) – also inactivates pancreatic lipase – PPI useful for early phase

Bacterial Overgrowth

-Bacteria growth determinants

Gastric acid, pancreatic enzyme, enterocyte turnover, antegrade peristalsis , ileocaecal valve

-Small bowel bacteria – usually only have one small aerobic population

-Large bowel – anaerobic

-Colonic bacteria can help in SBS by metabolising and recovering malabsorbed nutrients – ie improve absorption

-Small bowel overgrowth (inflammation) can lead to malabsorption

- Inflammation reduces absorbtive area – protein loss

Diet Composition and Diarrhoea

-Carbohydrates are the major cause of diarrhoea due to osmotic load after breakdown by pancreatic enzymes

-In the colon bacteria breakdown malabsorbed substances to cause further osmotic load

-Retained colon able to absorb fluid, electrolytes, short chain fatty acids

-Protein and Fat – less osmotic load

Consequences of Short Bowel

Likelihood of resuming an oral diet depends on:

-Length of remaining small bowel

Intact duodenal >200cm of jejunum and intact colon eventually able to eat

-Remaining segments of bowel

Proximal small bowel resection – protein, CHO, Fat absorption - Ileum able to compensate

Distal (ileum) small bowel resection – B12/Fat/Bile salt malabsorption if <100cm resected – liver able to compensate. Loss of ileal break.

-Presence of the colon and intact ICV

-Intestinal adapation

Intestinal Rehabiliation

Early Management

-Parenteral Nutrition

-Fluid and electrolyte balance

-H2RA or PPI to prevent gastrin hypersecretion which inactivate pancreatic enzymes

-Fish oil based IV lipid emulsion

-Enteral feeding – complex enhances adapation (rather than elemental). Continuous tube feeding helpful postoperatively

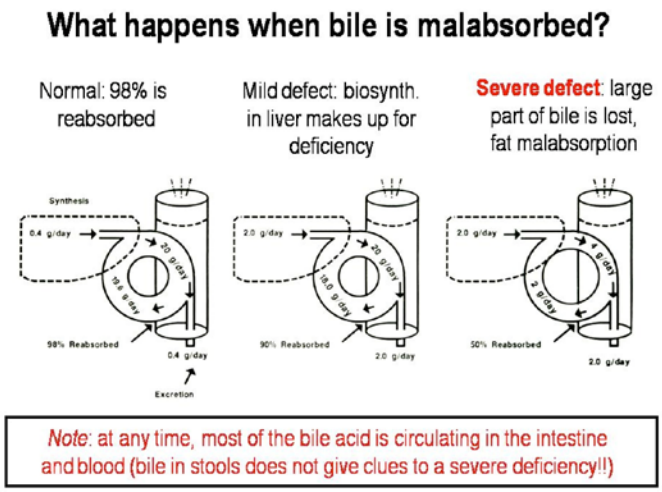
Limited ileal resection

-<100cm ileum resected able to eat solid food

-Chlolestyramine for bile salt malabsorption

- Questran Lite
- Colestipol

-B12 injections IM monthly



Extensive Small Bowel Resection

-Transition from Parenteral to Enteral feeding

-Intestinal Adaptation not complete

-Calcium, Zinc, Fat soluble vitamins (ADEK) monitor 3 monthly

-Vitamin B12

-Fat malabsorption – increased oxalate absorption -> Calcium Oxalate stones

-H2 Blockers/PPI and Octreotide inhibit excess gastric or pancreatic secretion

-Octreotide

>reduces fluid losses but also decreases splanchnic protein synthesis and may interfere with adaptation

>increases Small bowel transit

>increases risk of gallstones

-Loperamide

-Thickening agents

>But have CHOs – may stimulate SBBO

-Growth Factors

>GLP-2 eg Teduglutide - modest effect for severe SBS and intestinal failure – reduces time requiring parenteral nutrition

>Glutamine and Growth Hormone – conflicting results

2. Post-Cholecystectomy Syndrome

-Presence of symptoms after cholecystectomy

-Caused by alterations in bile flow due to loss of GB reservoir

>Continuous flow of bile into Duodenum – leading to Oesophagitis and Gastritis

>Diarrhoea and colicky pain

-First described in 1947 by Womack and Crider

>Non GB pain that persists

>Development of GB pain that is new

-Development of symptoms eg gastritis or diarrhoea post cholecystectomy

-Cholecystectomy was the treatment of choice since 1860 for biliary colic and cholecystitis

-80-95% successful if stones present

-40% failure rate if no stones present

-500,000 Cholecystectomies performed in USA per year

-10% develop PCS

-Diagnosis improving with improved imaging – eg functional disease of the biliary tract/SOD etc

PCS: Epidemiology

- Organic vs Functional
- 5-30%
- Ddx: Functional disorder, Peptic ulcer disease, wound pain, stones, subhepatic fluid collection, incisional hernia - ?bile reflux
- Urgent operations – higher risk of PCS
- Predictors? – studies inconsistent
- Age – 20-29y 43%; 30-39% 27%; 40-49y 21%; 50-59% 26%; 60-69y 31% - rare >70y

PCS: Aetiology

- Bile is thought to be the cause
- Stomach or Duodenal irritation -> Diarrhoea
- Gastric bile acid increases

PCS: Ddx

-Gallbladder remnant and cystic ducts: Residual or reformed gallbladder, stump cholelithiasis, neuroma

-Liver: Fatty liver, hepatitis, hydrohepatosis, cirrhosis, chronic idiopathic jaundice, Gilbert, Dubin Johnson, Hepatolithiasis, PSC, Cysts

-Bile Duct: Cholangitis, adhesions, strictures, trauma, cysts, CCA, obstruction, CBD stone, dilatation, dyskinesia, fistula

-Peri-ampullary:SOD dyskinesia/spasm/hypertrophy, SOD stricture, papilloma, cancer, pancreatitis, PD stone, pancreatic Cancer

-Oesophagus: Aerophagia, diaphragmatic hernia, hiatus hernia, achalasia

-Stomach: Bile gastritis, PUD, gastric Cancer

-Duodenum: Adhesions, diverticulosis, IBS

-Small Bowel: Adhesion, incisional hernia, IBS

-Colon: Constipation, diarrhoea, incisional hernia, IBS

-Vascular: Intestinal angina, coronary angina

-Nerve: Neuroma, intercostal neuralgia, spinal nerve lesions, sympathetic imbalance, neurosis, psychological

-Other: Adrenal cancer, arthritis, thyrotoxicosis, foreign body – gallstone/surgical clip

Presentation

- Wide range of symptoms
- RUQ pain
- Jaundice
- Fever
- Diarrhoea
- Nausea
- Bloating
- Gas

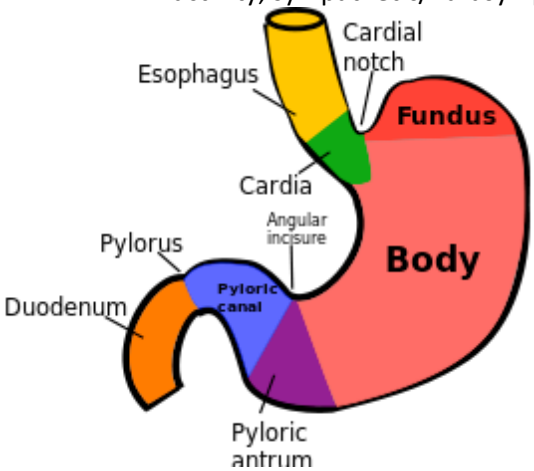
Workup

- Tailor according to clinical suspicion
- Bloods - CBC, U&E, LFTs, Cardiac enzymes
- CXR
- ECG/ETT
- OGD
- USS? CT? MRCP ? EUS Biliary scintiscan
- ERCP +/- sphincterotomy – biliary manometry?
- Morphine provokation, Secretin stimulation – check for PD dilatation, signs of chronic pancreatitis

3. Dumping Syndrome

Stomach

- Stomach –capacity 1.5-2L
  - Cardia
  - Fundus
    - reservoir
  - Body
  - Pylorus
    - Churns and mixes
- Motility
  - Myogenic, circulating hormones, neural activity, sympathetic/Parasympathetic

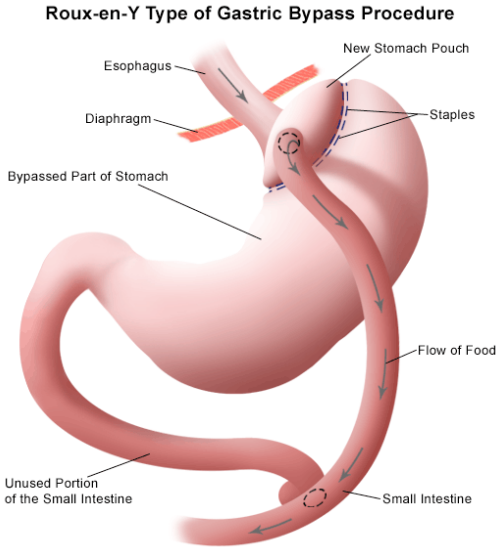


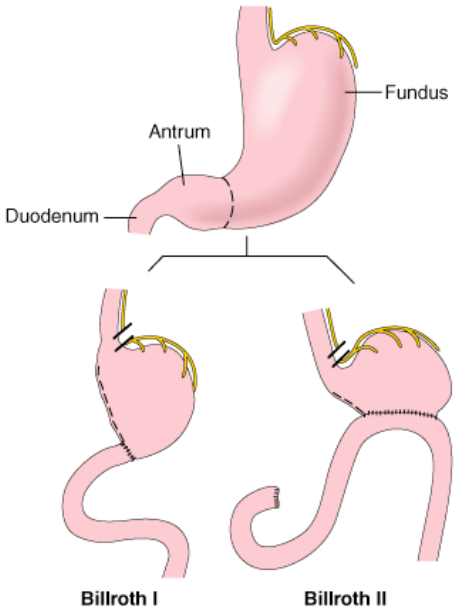
Post-gastrectomy Syndromes

- Small Capacity
- Dumping Syndrome
- Bile gastritis
- Afferent Loop syndrome
  - kinking
- Efferent Loop syndrome
- Anaemia
- Metabolic bone disease

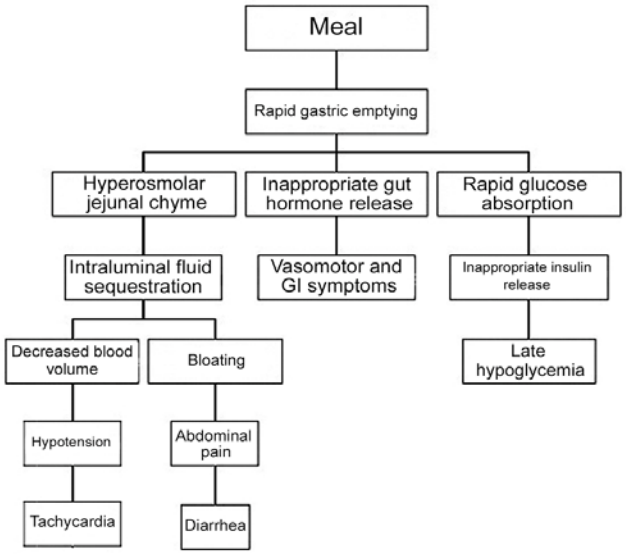
Gastrectomy

- Roux-en Y gastric bypass
- Bilroth I
- Bilroth II





Pathophysiology



How common is it?

- Clinically significant in 10% after any type of gastric surgery
- Up to 50% of Laparoscopic roux-en Y gastric Bypass
- More common in types of surgery
  - Vagotomy (for peptic ulcer disease)
  - Pyloroplasty
  - Gastrojejunostomy
  - Laparoscopic Nissen fundoplication
- Less elective gastric surgery for PUD these days
- Bariatric surgery
  - Neurologic Immune Restoration Inflammatory Syndrome
  - Octreotide helps
  - Due to pancreatic islet hyperplasia which may require resection

Digestion

- Body of stomach – chemical digestion by acid and proteases
- Food transferred to Antrum – high amplitude contractions
- Food broken down in to 1-2mm
- Pass through pylorus – this stops larger particles going through
- Gastric emptying depends on
  - Fundic tone
  - Antropyloric mechanisms
  - Duodenal feedback
- All affected by surgery

Surgery

- Gastric resection
  - Reduces fundic reservoir
  - Less accomodation (stretching)
- Vagotomy
  - Increases gastric tone
  - Limiting accomdation
- Pylorus removed/bypassed
  - Increased gastric emptying
- Bypass eg Gastrojejunostomy
  - Duodenal feedback inhibition of gastric emptying lost

- *Accelerated gastric emptying is the hallmark of Dumping syndrome*
- Gastric mucosal function altered – less secretion, enzymes, hormones affected

Early Dumping

- Early dumping and reflux gastritis
  - Less common with partial/segmental gastrectomy
  - More common with distal surgery
- Truncal vagotomy, patrical gastrectomy, roux-en Y gastrojejunostomy - 41% developed dumping within first 6 months
- Severe dumping is rare <5%
- Occurs in 45% of those malnourised and who have had complete or partial gastrectomy
- Rapid emptying – Diarrhoea
- 30-60 min after a meal
- Hyper-osmolar contents into small bowel
- Fluid shifts – intravascular volume contraction – vasomotor symptoms -> tachycardia, light headedness
- Small bowel distension – bloating, cramping
- This simplistic hypothesis has been called into question
- More likely due to interplay of gut hormones
  - Enteroglucagon
  - Peptide YY
  - VIP
  - GLP-1
  - GIP
  - Neurotensin
- Causes sympathetic overdrive
- ?Role of serotonin
- Ileal brake – mediated by the above

Late Dumping

- 1-3 hours after a meal
- Hyperinsulinaemic hypoglycemia
- CHO into proximal small bowel rapid absorption of glucose
- Insulin stays high – then get hypoglycemia – Incretin effect
- GIP, GLP-1 exaggerated response after gastrectomy

Late Dumping: Hypoglycemia

- OGTT – Hyperinsulinaemic Hypoglycemia
- Gastric scintigraphy – delayed then accelerated gastric emptying

Clinical Presentation

- Gastrointestinal
  - Early satiety
  - Crampy abdominal pain
  - Nausea
  - Vomiting
  - Explosive diarrhoea
  - Borborygmi
  - Hunder
- Vasomotor
  - Diaphoresis
  - Flushing
  - Dizziness/Faintness
  - Palpitations
  - Intense desire to lie down/Fatigue
  - Headaches
  - Syncope
  - Poor concentration
  - Decreased consciousness

Sigstad's Diagnostic Symptoms

- Symptoms and points
  - Shock +5
  - Near syncope, impaired consciousness +4
  - Desire to lie or sit +4
  - Breathlessness +3
  - Weakness/exhaustion +3
  - Sleepiness, drowsy, apathy +3
  - Palpitation +3
  - Restlessness +2

Medical Treatment

- **Acarbose**
  - Alpha-glycoside hydrolase inhibitor – interferes with carbohydrate absorption
  - Increases post prandial glucagon-like peptide 1 levels -> decrease in insulin release
  - Causes diarrhoea – fermentation of unabsorbed carbohydrates and flatulence
- **Octreotide** 50mcg/ bd or tds 30min premeal – or LAR
  - Short term success.
  - Synthetic analogue of Somatostain
  - "Endocrine brake" – inhibits insulin and several gut derived hormones
  - Slows gastric transit time
  - LAR improved QoL but short acting better for late dumping symptoms

Surgery

- Prevention preferrable
- Proximal Vagotomy preferred over antrectomy and truncal vagotomy
- Pyorus preserving gastrectomy
- Examples to fix the problem
  - Bilroth II to Bilroth I
  - Surgical narrowing of the gastrojejunal stoma

Diet

- Daily energy intake divided into 6 meals
- Fluid intake with meals is restricted (within 30 min)
- Avoid simple sugars
- Avoid milk products
- Protein and fat increased to balance drop in carbs
- Lying supine 30min delays gastric emptying and increase venous return – less syncope
- Dietary fibre to treat hypoglycaemia – prolong bowel transit delayed glucose absorption

Summary

- Generally post operatively after resection most patients are well
- Small subset of severe disease
- Treatment depends on site and length of resection
- Adaptation can take time