Session 1: Prof William Young

1.	Q: Due to delay in recognising and workup, a patient who has been hypertensive and hypokalemia since age 32, only managed to get ct adrenal done when she was 43 y/o which reported 1.2cm left adrenal nodule. She refused for surgery, thus was treated medically. she somehow changed her mind, keen for surgery, and therefore a repeat CT adrenal done 2 years later similarly report left adrenal nodule. In this case, can we safely proceed surgery without avs? Prof W. Young: If I was seeing this patient in the clinic next week, I would proceed with AVS.
2.	Q: As what I observe, Its a common practice that physicians order plasma and urine catecholamine to hunt for ppgl instead of plasma metanephrines, would these investigations should be changed to plasma metanephrine and normetanphrine instead? Prof W. Young: Plasma catecholamines is frought with false positive testing. Fractionated metanephrines is a much better test.
3.	Q: For lipid poor small adenoma, is there a cut off of size to recommend surgery or should we wait for it to clinically apparent Prof W. Young: Typically >1.5 cm - the larger, the more concerned I am.
4.	Q: Hi prof, in patient with adrenal incidentaloma which is lipid poor, however biochemically screen negative for pheochromocytoma, will you consider further workup eg chromogranin A, functional imaging, before sending the patient for surgery? Prof W. Young: No. We provide low-dose adrenergic blockade to all patients with normal biochemistry in the setting of lipid poor adrenal masses
5.	Q: We only have unfractionated plasma and urine metanephrines and samples are processed only once a month and expensive. In patients with profound spells, would doing imaging and looking for a suspicious lesion be reasonable before doing the biochemical test for pheo? CT scans are much cheaper than the biochemical testing. Thank you. Prof W. Young: Oh, that is interesting! If your suspicion for pheo is high, and in your unique clinical setting, I think you could justify a "CT-first" strategy.
6.	Q: We don't have phenoxybenzamine nor doxazosin, will terrazosin be useful fore preop pheo surgical prep Prof W. Young: Yes, terazosin will work just fine.
7.	Q: How can we diagnose hyperaldosteronism if already developed CKD? Prof W. Young: Measurements for aldo and renin are valid even with stage 4 CKD.
8.	Q: Would we screen for PA in a young ESRF patient with hypokalemia? Would the intepretation of ARR be affected? Prof W. Young: "Maybe" I would go ahead and test. It depends in part on the pathogenesis of ESRF and whether there is concurrent renovascular component.

9.	Q: Some ppxs with PA have first or intermittent Aldo 5-10 ng/dl (K normall, renin suppressed). Why is that? How do you deal with that? What is the max dose of eplerenone you have used for PA? Prof W. Young: PA is a spectrum from low renin & lowish aldo to slowly rising aldo. In addition, PA must start at some point. Patients aren't normal on day 1 and have marked PA on day 2.
10.	Q: What are the investigation use for Long standing PA with non suppressed DRC from atherosclerosis related to Renal artery stenosis or in CRF A: This is problematic to categorize. For sure it happens.
11.	Q: Is there clear benefit for unilateral adrenalectomy vs medical therapy for unilateral PA? Many patients are reluctant to undergo AVS nor surgery. Prof W. Young: Yes, there is a clear benefit to surgery over chronic MRA treatment--see SPARTACUS. Having said that, I never "force" a patient to have AVS. My role is to educate them on their options.
12.	Q: In a 50 yo patient with PA, with a 2cm left adenoma, HU 17, right normal . Significant hypoK, very high aldo. 1. Can we skip AVS as looks clear cut unilateral PA, although age 50. Should we screen for phaeo as well as the HU is 17? She is asymptomatic. Prof W. Young: This is the type of patient where you can consider skipping PA. But the patient would need to understand that there is still a possibility (although unlikely) of contralateral disease. 2. I would screen biochemically for pheo in nearly all patients with unenhanced CT attenuation >10 HU. 3. Having said all of that, a key test here is to screen for subclinical Cushiing syndrome with an overnight dexamethasone suppression test. If this patient has subclinical cortisol secretory autonomy, that will become the priority. We have great medical treatment for aldo excess, but not cortisol excess--on top of that in the settiing of subclinical CS and PA, it is usually a unilateral indeternated density nodule co-secreting both and AVS is not needed.
13.	Q: Hi Prof. I have a patient with paraganglioma and underwent surgical removal. Post-op, the plasma normet remains 1.5- 1.7x of UL, Ga68 Dota is negative, genetic screen negative. What should I do? Prof W. Young: 1. review the med list again; 2. make sure patient is not taking any supplements not listed; 3. remember that the false + rate is 15% and it increases with age; 4. with a negative DOTATATE, I would probably follow with serial biochemistry and recheck CT in 1 yr of the region of interest and then perhaps a DOTATATE in 2 yrs if labs are persistently abnormal.
14.	Q: How fast does K normalize after adrenalectomy for PA Prof W. Young: Usually within 1 to 4 days. The main concern postop is HYPERKALEMIA - this occurs in 5% of patients and we check blood potassium weekly x 4.
15.	Q: when would you consider genetic testing in confirmed PA patients? Prof W. Young: Hardly ever. Genetic cases of PA, although interesting, are rare. So, would do genetic testing if PA less than age 20 or if +FHx of PA.

16.	Q: Which among the options for confirmatory testing (saline infusion, oral sodium) for primary aldosteronism is the most preferred? Prof W. Young: Depends on the center. In general there are less false negatives with the 24-hr urine approach.
17.	Q: In cases incidentaloma that has traits of suspected pheochromocytoma, but no hypertension and normal biomarkers (include plasma metanerphrine and urine catecholamine), how should we follow up these case? When should we consider for surgical treatment? Prof W. Young: I consider surgical resection in all lipid poor adrenal masses >1.5 cm. Lipid poor adrenal masses can be nothing good. This is where ACC comes from. If a patient declined surgery, I would probably follow them for 20 yrs before I would be reassured.
18.	Q: I found some patients who have CT look like PBMAH but hormonal testing fitted to co-secretion of aldosterone and cortisol. 1. What is your recommend protocol for AVS? 2 I have tried spironolactone 50 mg during work up and found that patients showed hypoaldosteronism>> What am I wrong? 3. Do you recommend genetic mutatition testing for PA cases? What are the rationals? Prof W. Young: PBMAH is a CT diagnosis. Some patients with PBMAH do co-secrete aldo and cortisol. There is never a reason to do AVS in PBMAH--it is always bilateral. I don't understand your comment on SPL. See answer to above question about when to do genetic testing in patients with PA.
19.	Q: How we manage the patient with increase ARR test but negative confirmation test (NaCl test)? Prof W. Young: Such patients may have very mild PA or "pre-PA". We typically add a MRA to their treatment program
20.	Q: How should we aggressive working up for atherosclerosis for patients diagnosed for PA? Prof W. Young: No special protocol in this regard. Basically CV testing should be done if clinically indicated.
21.	Q: How do we manage the side effects of giving spironolactone long-term (gynecomastia, menstrual irregularities, etc)? Prof W. Young: If and when these side effects develop, we switch to eplerenone. If eplerenone is not available, we stop SPL and then re-introduce a couple months later at a low dose (eg, 12.5 mg daily) and add amiloride with the goals of serum potassium of 4.5 mEq/L and PRA >1 ng/mL/hr or PRC >8.
22.	Q: I have a pheo patient with ejection fraction of only 25%, became tachycardic on terrazosin, will ivabradine be effective for the tachycardia? I am afraid of giving beta blocker due to low EF

	Prof W. Young: We work closely with cardiology in such cases. Certainly a CCB may be effective. Also in such a case, we consider alpha-methly-para-tyrosine (Demser; metyrosine), which blocks tyrosine hydroxylase and prevents production of catechols. In about 50% of patients with a catechol cardiomyopathy the EF improves with adrenergic blockade or Demser.
23.	Q: For lipid poor adrenal incidentaloma with negative biochemistry for pheochromocytoma, what is your the HU threshold to consider that it may be a biochemical negative pheo rather than a lipid poor adrenal adenoma? Prof W. Young: Between 10 and 20 HU is indeterminate. When >20 HU a lipid poor adrenal mass is confirmed and resection should be considered. Lipid poor adrenal masses can be nothing good. See answer to one of the previous questions.
24.	Q: How do you monitor patients with pheo who require levodopa for parkinson? Prof W. Young: If the levodopa cannot be stopped and the clinical suspicion for pheo is high, simply do CT of abdomen and pelvis--85% of catechol-secreting tumors are in the adrenals and 95% between the diaphragm and pubis.
25.	Q: Does the use of alpha-blockade (phenoxybenzamine/ terazosin) affect plasma metanephrines assessment? This is extrapolating from the mechanism by which clonidine suppresses extraneuronal norepinephrine release. hence alphablockers may work to promote a false positive Prof W. Young: Catechols rise in the first 2 days of alpha-adrenergic blockade, but fine after that.
	Q: In the context of the question above, could you have a tumor arising from the cortex (e.g. APA with hyper aldo) AND a tumor from medulla like a pheo at the same time? Prof W. Young: Yes. We published an article on this a few years ago.
	Q: I have a pt admit, we suspect he have Pheo, we get start scan for him: left adrenal mas 12mm with density of 19UI. and we dosage urine cathecolamine also increase and ration renin/aldosterone also increase. Prof W. Young: I would need actual lab data on this one in order to provide any insights.
	Q: If patient has cardiomyopathy (likely as a result of the PA) limiting salt loading for diagnostic testing for suspected PA in view of risk of fluid overload, would you do clonidine suppression test? Prof W. Young: If you can't sodium load, this is where you need to rely on baseline levels of aldosterone and renin
	Q: is there any test superior or preferable in testing PA in ckd 4 or 5 ? do u think its still beneficial for adrenalectomy (in identified unilateral case) if alrd in ckd 5.

	Prof W Young: These are very difficult cases because if you send for surgery, they will not longer be hyperfiltrating at the kidney and will likely progress to ESRD and need dialysis. With regard to your question, simply measure blood aldo and renin.
	Q: Could unexplained progressive increase in potassium with low normal sodium over 5 months post-adrenalectomy for unilateral PA be due to hypoaldosteronism? Prof W. Young: Yes. This can happen in longstanding severe PA. If hyperkalemic, we would typically treat with low-dose fludrocortisone--e.g., half of a 0.1 mg tab daily.

Session 2: Assoc Prof Joanne Ngeow

1.	Q: As the disease menifestation is related to pathogenic mutations penetrance, is there any way to asses whehter a particular proband seeking genetic counseling will be affected by the disease or not? Assoc Prof Ngeow: Unfortunately - our recommendations are largely based on pooled data rather than specific - i.e. we know probabilities based on a gene/ a variant etc but not at individual level This is the importance of therefore data sharing as a community for us to then have enough "power" to better understand genotype -phenotype. I will say that for RET - do have a good grasp of which are the "bad" mutations but for the other genes - we aren't yet at the stage where we can be "variant specific" in our recommendations.
2.	Q: If some genes have <1% frequency, will be the logical to screen those genes which may increase the cost for the patient? How to make convincing case for including appropriate genes in a panel? Assoc Prof Ngeow: Typically they will be included together with the common ones - in that way the cost is mitigated. Knowing the local population data is a good way to making the case
3.	Q: In the case of a patient with a SDHx mutation (identified following the presentation of recurrence of HNPGL), who has children, at what age would you recommend genetic testing for their children? If one of the children tests positive for the mutation (asymptomatic), would you recommend interval CT scans and/or plasma metanephrines for monitoring? Assoc Prof Ngeow: This is a not a straightforward one. The guidelines do say to offer testing and screening after but the costs in ASEAN is quite prohibitive. So, it makes it hard but especially for SDHB and even SDHD - we have had several children with pheo - as young past 5 years old - so it isn't always straightforward. We do offer testing the kids and screening if positive because of above but there are challenges doing this locally.
4.	Q: Is there any role in detecting somatic mutation in PPGL? Assoc Prof Ngeow: It is interesting on a research basis for knowing if we see teh loss of the other allele (LOH) etc but clinically not super useful and expensive, so we don't do it. SDHB IHC can be helpful and a cheaper options but like all IHC - there are issues with variable reporting etc .. so more important than any of these- it is to test them all germline will do! :)

5.	Q: If patients with PPGL have negative genetic testing (blood sample), how sure we are about the result? do we need to keep the blood sample for future reference if more pathogenic genes are confirmed? Assoc Prof Ngeow: Depends on the lab - it is important to check what genes are on the panel and if you can what coverage for each gene is "covered" - some genes like SDHD can be tricky for NGS panels. So working with reputable labs is important. If there is a very strong FHX then often my team would hunt very hard for ensuring there isn't any missed because of testing limitations. If it is not highly suspicious - would consider it sporadic esp older patients with no Fhx. We bank all our cases in Singapore for futher research and yes it is sometimes needed to call patients back .. for example in the era pre SDHx- folks only had VHL or RET or both - so if you have patients with historically only that tested then these would then need to have SDHx today to be complete.

Open questions (not answered in chat / live)

1. Anonymous attendee: Thank you very much for the intersting talk. How can you define that pheochromocytoma is NE predominate or E predominate (do you use any ratio or compare with the reference range)?

2. Anonymous attendee: Are hybrid hormone levels are affected by medications?

3. Dear Prof William, I would like to ask do we need to alpha blockade for nonfunctional head and neck paraganglioma prior op?

4. Anonymous attendee: Hi Dr Young, out of all the lipid poor adrenal masses that you've sent for adrenalectomy, is there any data on the proportion that came back positive for a pheo vs an adenoma?

5. Just a quick question for Prof Young - about lipid poor adenomas - after resection, roughly how many turn out to be phaeos vs adenomas?

6. Anonymous attendee: Hi Prof Young, for large phaeo > 4cm , that are not functioning , do u still cover with alpha blockade pre -op ?

7. Anonymous attendee: Hi Prof Young, what are your thoughts on screening for hormonal excess in a subcentimetre incidental adrenal nodule and follow up for them? Thank you!

8. Could the pregnancy PPGL pt have tumor removal during her C section? Or was it felt to be technical unfeasible/ risky?