Doctor, Are You Helping or Harming?

Inter-Hospital Geriatric Meeting
26th February, 2010
Dr CK Shum
Supervisor: Dr KF Tam
Division of Geriatrics
Department of Medicine
Queen Elizabeth Hospital
Mr TC Shum

- 83 years old gentleman
- Chronic smoker, non-drinker
- Lives with family and maid
- Independent activities of daily living
- Walks unaided
- Out going
Mr TC Shum

• **Past Medical History:**
  – Chronic atrial fibrillation with rapid ventricular response, refused warfarin, on aspirin and digoxin
  
  Echocardiogram (1993): left ventricular function satisfactory, trivial tricuspid and mitral regurgitation, no mitral stenosis
  – History of thyrotoxicosis with radioactive iodine (RAI)

  **Follow up in General Out-Patient Clinic (GOPC)**

• **Medications:**  
  - Aspirin 80mg OM  
  - Digoxin 187.5 microgram daily  
  - Pepcidine 20mg BD
Mr TC Shum

- Noted to have **runny nose and cough** for 4 days
- No fever or shortness of breath
- No recent travel / close contact with sick people
- Attended GOPC on 9/11/2009
- Given:
  - Piriton (chlorpheniramine) 4mg tds
  - Cocillana 10ml QID
  - Dequadin 250 microgram tds prn
On 15/11/2009 at home
At noon before lunch
Rose up from chair & walked to the toilet
 → Dizziness with transient vertigo, no tinnitus
 → Rapidly followed by loss of consciousness
 → Fell down, landed on both knees and then lay on the floor
 → Regained consciousness after around 1 min
Attained by daughter (who was at home at that moment)
Got up by himself
Noted left knee swelling and pain
1st episode of syncope
History

- No limb weakness / numbness / slurred speech
- No features of convulsion
- Associated with dull aching non-exertional retrosternal chest discomfort with no radiation
- No palpitation
- No shortness of breath / sweating
- No abdominal / urinary symptoms
- No fever
- No ear pain / discharge
- Not related to head / neck / arm movement
What are the Differential Diagnoses in this Patient?

**Cardiac arrhythmias as primary cause**
- Sinus node dysfunction (including bradycardia/tachycardia syndrome)
- Atrioventricular conduction system disease
- Paroxysmal supraventricular and ventricular tachycardias
- Inherited syndromes (e.g., long QT syndrome, Brugada syndrome)
- Implanted device (pacemaker, ICD) malfunction
- Drug-induced proarrhythmias

**Structural cardiac or cardiopulmonary disease**
- Cardiac valvular disease
- Acute myocardial infarction/ischaemia
- Obstructive cardiomyopathy
- Atrial myxoma
- Acute aortic dissection
- Pericardial disease/tamponade
- Pulmonary embolus/pulmonary hypertension

**Cerebrovascular**
- Vascular steal syndromes

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**Chronic atrial fibrillation**

**On Digoxin**
- Digoxin toxicity?

**Underlying atrial fibrillation**

**Advanced age**
- Chest discomfort during syncope

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What are the Differential Diagnoses in this Patient?

**Neurally-mediated (reflex)**
- Vasovagal syncope (common faint)
  - classical
  - non-classical
- Carotid sinus syncope
- Situational syncope
  - acute haemorrhage
  - cough, sneeze
  - gastrointestinal stimulation (swallow, defaecation, visceral pain)
- micturition (post-micturition)
- post-exercise
- post-prandial
- others (e.g., brass instrument playing, weightlifting)
- Glossopharyngeal neuralgia

**Recent flu symptoms**

**Syncope after rising from chair & walking to toilet**

**Orthostatic hypotension**
- Autonomic failure
  - primary autonomic failure syndromes (e.g., pure autonomic failure, multiple system atrophy, Parkinson’s disease with autonomic failure)
  - secondary autonomic failure syndromes (e.g., diabetic neuropathy, amyloid neuropathy)
  - post-exercise
  - post-prandial
- Drug (and alcohol) induced orthostatic syncope
- Volume depletion
  - haemorrhage, diarrhoea, Addison’s disease

**ESC Guidelines on Management (Diagnosis and Treatment) of Syncope – Update 2004. Europace (2004) 6, 467-537.**
Discussion: What are the Differential Diagnoses in this Patient?

**Disorders without any impairment of consciousness**
- Falls
- Cataplexy
- Drop attacks
- Psychogenic pseudo-syncope
- Transient ischaemic attacks (TIA) of carotid origin

**Disorders with partial or complete loss of consciousness**
- Metabolic disorders, including hypoglycaemia, hypoxia, hyperventilation with hypocapnia
- Epilepsy
- Intoxications
- Vertebro-basilar transient ischaemic attack

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Physical Examination

• General Examination
  – BP 158/64, P 65, SpO2 100% RA
  – No fever
  – H’stix 7.5
  – Body Weight 55.1kg, Body Height 1.70m, BMI 19.1
  – Mentality: conscious, alert, obeys commands
  – Hearing impairment (right > left ear)
  – Able to read small prints on newspaper with spectacles
  – No pallor, jaundice or cyanosis
  – No goiter clinically
  – No external wound
  – Hydration satisfactory
Physical Examination

• Cardiovascular Examination
  – No postural hypotension
  – Pulse irregularly irregular
  – Heart sound dual, no murmur
  – JVP not elevated, no peripheral edema
  – No carotid bruit

• Chest clear

• Abdomen soft, non-tender
Physical Examination

• Neurological Examination
  – Tone normal
  – Power 5/5 in 4 limbs except left knee flexion / extension 4/5 (limited by pain / swelling)
  – Jerks normal, plantar downgoing
  – Sensation: proprioception intact
  – Cranial nerve examination: unremarkable
  – No extra-pyramidal signs
  – No myelopathic hand signs
  – No cerebellar signs

• Musculoskeletal Examination
  – Left knee redness, swelling & tenderness, range of motion (0-100°)
What will You Do to Investigate further?

- Blood tests:
  - CBP
  - LRFT, CaPO4
  - Cardiac enzymes
  - Digoxin level
  - TFT
- ECG
- CXR
- XR knees
Investigation

- **Complete Blood Picture (CBP):**
  - Hb 12.7 ↓
    - ↑ MCV (100.1 fL), ↑ MCH (34.6 pg)
  - WBC Normal
  - Plt 136
- **Na 134 ↓ (136-145 mmol/L)** K Normal
- **Cr 79 (65-110 umol/L)** Urea Normal
- **Liver function test (LFT):** Normal
- **Troponin I < 0.03 ng/ml x 2**
- **CK 511 IU/L ↑**
- **LDH 345 IU/L ↑**
- **ECG:** AF, 60/min
Chest X-Ray
On digoxin 187.5 microgram daily
- ↑ Digoxin dose 62.5 → 125 → 187.5 microg daily because of inadequate rate control in GOPC
Discussion:

Is it Digoxin Overdose?

1. Yes
2. No

- Appropriate Timing of Therapeutic Drug Monitoring
Discussion:

Serum Digoxin Concentration (SDC)

• Appropriate timing for therapeutic drug monitoring
  – Steady state concentration (7-14 days after initiating therapy)
  – At least 6-8 hours after last digoxin dose / trough level (distribution phase of digoxin)

Contemporary Use of Digoxin in the Management of Cardiovascular Disorders *Circulation*. 2006; 113:2556-2564
Digoxin Level of this Patient

Collect Date: 16/11/09
Collect Time: 07:18
Regist Date: 16/11/09
Regist Time: 08:41
Request No.: J2980597

Conversion Factor
1 nmol/L = 0.78 ng/mL

Therapeutic Drug Monitoring

Serum Digoxin

Footnotes:
- Please note that digoxin specimen for monitoring should be taken at least 6 hr after the last dose. Hydrocortisone and pentoxifylline cause falsely elevated digoxin results at concentrations of the recommended daily dose.

Reason medicine not administered
F-FASTING R-PATIENT REFUSED W-WITHHELD V-VOMITTING A-ABSENT FROM WARD

<table>
<thead>
<tr>
<th>DATE</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Freq.</th>
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<tbody>
<tr>
<td>15/11</td>
<td>Digoxin</td>
<td>187.5 microgram daily</td>
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DATE OFF/Sign. | Duration | Sign. |
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Appropriate Timing for Therapeutic Digoxin Monitoring
Discussion:

Is it a Normal Digoxin Level?

1. Yes
2. No

• Appropriate Therapeutic Range (provided by the Laboratory)
Discussion:

Serum Digoxin Concentration

- **Old range:** 1.0-2.5 nmol/L (0.8-2.0 ng/mL)
  
  Based on risk of digoxin toxicity not effectiveness
  Toxic symptoms much more common (>2.5 nmol/L)

- **New range:** 0.6-1.2 nmol/L (0.5-1.0 ng/mL)
  
  How about the new range? Improve Outcome?

Which One is the Optimal / Safer Therapeutic Range of Digoxin?

Understanding the mechanisms and manifestations of digoxin toxicity helps in its management and treatment. *Drugs Ther Perspect* 2007; Vol. 23, No. 2
Discussion:

Digoxin
Discussion:

Digoxin

• Purified cardiac glycoside extracted from the foxglove plant, Digitalis lanata
• Used clinically for more than 2 centuries
• Treat edematous states, irregular heartbeats & heart failure
Effects of Digoxin

**Inhibits Na⁺-K⁺ ATPase → ↑ intracellular Na⁺**

**Inhibits Na⁺-K⁺ ATPase → ↑ intracellular Ca²⁺ → ↑ systolic contraction**

**Discussion:**

**Hemodynamic effects in heart failure**
- Increased cardiac output
- Decreased PCWP
- Increased LVEF

**Neurohormonal effects**
- Vagomimetic action
- Improved baroreceptor sensitivity
- Decreased norepinephrine serum concentration
- Decreased activation of renin-angiotensin system
- Direct sympathoinhibitory effect
- Increased sympathetic CNS outflow at high doses
- Decreased cytokine concentrations
- Increased release of ANP and BNP

**Electrophysiological effects**
- S-A node: slowing of the sinus rate
- Atrium: no effect or decreased refractory period
- AV node: slowed conduction
- Ventricle and Purkinje fibers: practically no electrophysiological effects at low therapeutic doses

**Improve baroreceptor sensitivity**

**↓ Circulating noradrenaline**

**↑ Vagal**

**↓ Sympathetic**

**Slowing SA pacing rate via ↑ vagal tone**

**Slowing AV node conduction**

Contemporary Use of Digoxin in the Management of Cardiovascular Disorders

*Circulation.* 2006; 113:2556-2564
Discussion:

Beneficial Effect of Digoxin

PROVED Study

RADIANCE Study

- ↓ Heart failure worsening
- ↑ Exercise Tolerance
- ↑ LV EF
- No Effect in Mortality

Contemporary Use of Digoxin in the Management of Cardiovascular Disorders

Circulation. 2006; 113:2556-2564
Discussion:

DIG (Digitalis Investigation Group) Trial

- Randomized, double-blind placebo-controlled trial
- Effects of digoxin in patients with heart failure [preserved systolic function (DIG-Main), reduced systolic function (DIG-Ancillary)] & normal sinus rhythm
  - ↓ hospitalization due to worsening heart failure
  - No effect in cardiovascular & all-cause mortality

Beneficial Effects of Digoxin

Hospitalization due to Worsening Heart Failure

DIG Trial

Contemporary Use of Digoxin in the Management of Cardiovascular Disorders
*Circulation.* 2006; 113:2556-2564
Rising Mortality with Increasing Serum Digoxin Concentration (SDC)

Discussion:

Post hoc analysis of DIG trial

Higher vs. Lower Serum Digoxin Concentration (SDC)

**Discussion:**

Lower Concentration
- ↓ All-cause and heart failure mortality
- ↓ Hospitalization for heart failure

Higher Concentration
- No advantage
- ↑ Toxicity but no greater efficacy

**DIG Trial**

Contemporary Use of Digoxin in the Management of Cardiovascular Disorders. *Circulation.* 2006; 113:2556-2564

Drug Treatment of Chronic Heart Failure in the Elderly. *Drugs Aging* 2007; 24 (12)
Serum Digoxin Concentration (SDC)
0.6-1.2 nmol/L (0.5-0.9 ng/mL)

Optimal Therapeutic Range
(Safe, improve left ventricular function, hemodynamics & neurohormonal profiles, reduce hospitalization & possibly improves survival)
Conclusion: Digoxin Overdose
ECG of the Patient
24 Hours ECG Monitoring (Holter) of the Patient

• Holter Result:
  – Average heart rate 60 beats per minute
  – Maximum R-R interval 3.66 sec
  – Slow atrial fibrillation
  – Isolated ventricular ectopics, no ventricular tachyarrhythmia
Discussion:

What is So Special in Our Geriatric Population?
Discussion: Digoxin Toxicity in Elderly

• More common
  – Age related declines in lean body mass & renal function
  – Atrial fibrillation & heart failure more common in elderly
  – Multiple comorbidities & polypharmacy more common in elderly & possible interaction with digoxin
龄相关的生理学变化，可能影响药代动力学

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<td>胃肠血流量</td>
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<td>胃酸碱度</td>
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<td>胃肠蠕动性</td>
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<td>药物吸收的影响</td>
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<td>血浆白蛋白</td>
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<td>α-1 胰蛋白素</td>
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<td>总体水分量</td>
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<td>瘦体重</td>
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<td>肝血流量</td>
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<td>肾小球滤过率</td>
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<td>肾血流量</td>
<td>↓</td>
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<tr>
<td>肾小管分泌</td>
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</tbody>
</table>

↑ 表示增加；↓ 表示下降；⇔ 表示无变化。

Cardiovascular Drug Therapy in the Elderly: Theoretical and Practical Considerations. *Drugs Aging* 2003; 20 (6)
Discussion:

Digoxin Toxicity in Elderly

• More difficult to diagnose
  – Extra-cardiac symptoms non-specific / common in the elderly
    • CNS: confusion / delirium, hallucination, depression, anxiety, apathy, convulsion
    • Eye: visual disturbances, blurred vision, color vision
    • GI: nausea, anorexia, vomiting, diarrhea
    • Malaise, fatigue, weight loss, dizziness, falls

Clinical pharmacology and physiology conference: Digoxin toxicity in the elderly
Discussion: Digoxin Toxicity in Elderly

• More difficult to diagnose
  – Cardiac symptoms / signs
    • Palpitation, syncope
    • Bradycardia (atrial fibrillation with slow ventricular response, atrioventricular block), tachycardia (ventricular arrhythmia)
  – Hyperkalemia is a sign of severe digoxin toxicity
  – Look for rhythm disturbances (almost diagnostic):
    • New onset Mobitz type I atrioventricular block
    • Accelerated junctional rhythm with / without high level atrioventricular block
    • Non-paroxysmal atrial tachycardia
    • Bidirectional ventricular tachycardia

What Should be the Appropriate Dose of Digoxin for this Patient?

1. Digoxin 250 microgram daily
2. Digoxin 187.5 microgram daily
3. Digoxin 125 microgram daily
4. Digoxin 62.5 microgram daily
**Dose of Digoxin**

<table>
<thead>
<tr>
<th>HA Guidelines (Hong Kong)</th>
<th>ACC / AHA / ESC Guidelines</th>
</tr>
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<tbody>
<tr>
<td><strong>Atrial Fibrillation / Atrial flutter for Control of Ventricular Rate:</strong>&lt;br&gt;Digoxin 250-500 microg IV or 250 microg PO then Q8H PO for 3 more doses (total loading of 1000 microg)&lt;br&gt;Maintenance dose: <strong>125-250 microg</strong> daily (reduce dose in elderly &amp; chronic renal failure)</td>
<td><strong>Atrial Fibrillation for Control of Ventricular Rate:</strong>&lt;br&gt;Loading dose: Digoxin 250 microg IV each 2h, up to 1500 microg&lt;br&gt;Maintenance dose: digoxin <strong>125 - 250 microg</strong> daily</td>
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<tr>
<td><strong>Acute Myocardial Infarction &amp; Atrial Fibrillation / Atrial Flutter:</strong>&lt;br&gt;Digoxin 250 microg IV / PO stat, then 250 microg PO Q8H for 2 more doses as loading (total loading 750 microg)&lt;br&gt;Maintenance dose: <strong>62.5-250 microg</strong> daily</td>
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<tr>
<td><strong>Heart Failure:</strong>&lt;br&gt;No loading dose</td>
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</table>

*Handbook of Internal Medicine. COC (Medicine) Hospital Authority. 5th Edition 2008.*
Discussion:

Dose of Digoxin

- CrCl >120 ml/min  250 microgram daily
- CrCl 80-120 ml/min 187.5 microgram daily
- CrCl 30-80 ml/min 125 microgram daily
- CrCl <30 ml/min  62.5 microgram daily

Nomogram for Determining the Dose of Digoxin

- Graphical calculating device for determining the initial dose of digoxin in heart failure
- Adjusted for **body build** and **creatinine clearance**
- Target digoxin concentration **0.9nmol/L (0.7 ng/mL)**
- More accurate in predicting digoxin concentration [78% patients with <1.3nmol/L (1.0 ng/mL)]

*A Method of Determining the Dose of Digoxin for Heart Failure in the Modern Era. Arch Intern Med. 2006;166:2539-2545 (American Medical Association)*
Nomogram for Dose Determination

Discussion:

Discussion:

Can We just Purely Rely on this Nomogram for Dose Determination?

Change Digoxin Dose to 125 microgram daily?

Concomitant diseases
Drug interactions
Discussion: Conditions that may cause Increased Sensitivity to Digoxin

- Electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia, hypercalcaemia)
- Renal failure
- Congestive heart failure
- Acid-base imbalance
- Hypothyroidism
- Early phase post-myocardial infarction
Thyroid Function of The Patient

- Free T4: 3.6 (13.3-21.3 pmol/L) ↓
- TSH: 83.5 (0.27-4.20 mIU/L) ↑
- AM cortisol: 396 (138-635 nmol/L)
- Anti-thyroid microsomal antibody: Negative
- Anti-thyroglobulin antibody: Borderline, Titre 1:100

Impression: post RAI hypothyroidism
What Should be the Appropriate Dose of Digoxin for this Patient?

1. Digoxin 250 microgram daily
2. Digoxin 187.5 microgram daily
3. Digoxin 125 microgram daily
4. Digoxin 62.5 microgram daily
CT Brain (Plain) of the Patient
CT Brain (Plain) of the Patient
CT Brain (Plain) Report

- No acute intracranial hemorrhage noted
- No abnormal attenuation seen in brain parenchyma
- No hydrocephalus or extra-axial collection
- No midline shift demonstrated
- Chronic inflammatory change noted in right mastoid and right middle ear
Skyline View of XR Left Knee

Longitudinal Fracture of Left Knee
Discussion: Which Painkiller should be Given to this Patient?

1. Paracetamol (Panadol)
2. Non-Steroidal Anti-Inflammatory Agent (NSAID)
3. Weak Opioids (Doloxene)
4. Strong Opioids (Morphine, Pethidine)
### Drug Interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Effects</th>
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<tbody>
<tr>
<td>Non-potassium sparing diuretic</td>
<td>Hypokalemia, hypomagnesemia, promotes sodium pump inhibition</td>
<td>Increased risk of arrhythmias</td>
</tr>
<tr>
<td>Intravenous calcium</td>
<td>Increases myocyte calcium</td>
<td>Increased risk of arrhythmias</td>
</tr>
<tr>
<td>Quinidine, verapamil, amiodarone, propafenone, itraconazole, alprazolam, spironolactone</td>
<td>Reduce digoxin clearance and decrease volume of distribution</td>
<td>Increased SDC</td>
</tr>
<tr>
<td>Erythromycin, clarithromycin, potentially other macrolide antibiotics, tetracycline</td>
<td>Increase digoxin absorption by inactivating intestinal bacterial metabolism</td>
<td>Increased SDC</td>
</tr>
<tr>
<td>Propantheline, diphenoxylate</td>
<td>Increase digoxin absorption by decreasing gut motility</td>
<td>Increased SDC</td>
</tr>
<tr>
<td>Antacids, bran, cholestyramine, kaolin-pectin, metoclopramide, neomycin, sulfasalazine</td>
<td>Decrease digoxin absorption</td>
<td>Decreased SDC</td>
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<tr>
<td>Rifampin</td>
<td>Increases nonrenal clearance of digoxin</td>
<td>Decreased SDC</td>
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<td>Thyroid medications</td>
<td>Increase metabolic state</td>
<td>Decreased SDC</td>
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<tr>
<td>Sympathomimetics</td>
<td>Increase automaticity</td>
<td>Increased risk of arrhythmias</td>
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<tr>
<td>Succinylcholine</td>
<td>Extrudes potassium from cells</td>
<td>Increased risk of arrhythmias</td>
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<tr>
<td>β-Adrenergic blockers, nondihydropyridine calcium channel blockers, flecainide, disopyramide, bepridil</td>
<td>Decrease sinoatrial or AV node conduction</td>
<td>Increased risk of sinoatrial and AV block</td>
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<td>ACE inhibitors</td>
<td>May decrease renal function</td>
<td>Increased SDC</td>
</tr>
<tr>
<td>Nonsteroidal antiinflammatory agents</td>
<td>Decrease renal function</td>
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*Contemporary Use of Digoxin in the Management of Cardiovascular Disorders. *Circulation.* 2006; 113:2556-2564*
Discussion: Which Painkiller should be Given to this Patient?

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4. Strong Opioids (Morphine, Pethidine)

WHO Analgesic Ladder
Progress in Our Patient

Management

• 187.5 microg daily dose of digoxin was stopped and lower maintenance dose of digoxin 62.5 microg daily was restarted later
• Start low dose thyroxine 25 microgram daily
• Give paracetamol for pain control
Progress

• Seen by ENT Surgeon:
  – No acute ENT problem
  – Right aural polyp (incidental finding)

  – Management:
    • Early CT Temporal Bone (Plain) to exclude right middle ear pathology
    • Refer ENT SOPC for reassessment
Progress

- **Seen by Orthopedic Surgeon:**
  - Left knee extensor mechanism intact
  - XR Left Knee: longitudinal fracture of left patella
  - For conservative management
- **Management:**
  - Refer Orthopedics & Traumatology SOPC for reassessment
Progress

• In-Patient Rehabilitation delivered
  – Prosthetic & Orthotic (P&O): left straight knee brace applied and education taught
Progress

• In-Patient Rehabilitation delivered
  – Physiotherapy:
    • Ice therapy to left knee given
    • Walking with stick and knee brace independently
    • Walking stick available at home
Progress

• In-Patient Rehabilitation delivered
  – Occupational therapy:
    • Modified Barthel Index: 89/100
      (Bowel 10/10, Bladder 10/10, Personal hygiene 5/5, Toileting 8/10, Feeding 10/10, Dressing 10/10, Bathing 4/5, Transfer 15/15, Mobility 12/15, Stairs 5/10)
    • Independent up to dressing, transfer
    • Supervision for toileting, bathing, ambulation for safety purposes
    • MMSE: 28/30, GDS: 0/15
      (Orientation 9/10, Registration 3/3, Attention & Calculation 5/5, Recall 2/3, Language 8/8, Praxia 1/1)
Discharge

- No more dizziness or syncope
- Left knee pain and swelling improved
- Discharged on 20/11/2009
- Followed Up Geriatric Specialist Out-Patient Clinic (SOPC), Orthopedic SOPC, ENT SOPC
- Refer Geriatric Day Hospital (GDH) for Out-Patient Training
Post-Discharge

• Followed Up by Geriatric Team (on 9/12/2009, 6/1/2010):
  – No more dizziness / syncope / fall after discharge
  – BP 121/83, P 76 (on 6/1/2010)
  – Serum digoxin concentration (SDC) after reduced dose of digoxin (62.5 microg daily): 0.7 nmol/L
  – Gradually increase dose of thyroxine 25 → 50 → 75 microgram daily
  – Thyroid function: TSH 83.5 → 62.8 → 50.0 pmol/L (13.3-21.3 pmol/L)
Post-Discharge

• Followed Up by Geriatric Team:
  – **Medications** (on 6/1/2010):
    • Aspirin 80mg daily
    • Pepcidine 20mg daily
    • Digoxin 62.5 microg daily
    • Thyroxine 75 microg daily
  – **Echocardiogram** arranged to rule out structural heart disease
  – Plan to repeat **Holter** examination after thyroid function under control
Post-Discharge

• Followed Up by ENT Surgeon:
  – Large pulsating right aural mass with smooth surface blocking right external auditory canal
  – Left tympanic membrane intact
  – Nasoendoscopy: nasopharynx clear
  – CT Temporal Bone (Plain):
    • Soft tissue lesion in right middle ear cavity with bony erosion involving middle ear ossicles, scutum, bony wall of facial nerve canal, and possibly infero-lateral wall of right vestibule. It can be chronic inflammatory changes with cholesteatoma formation
    • Opaque right mastoid cells with sclerosis, suggestive of chronic inflammatory changes
CT Temporal Bone (Plain)

- **Management:** for observation at present
Post-Discharge

• Followed Up by Orthopedic Surgeon:
  – No pain & non-tender over left knee
  – Range of motion full
Post-Discharge

• After a course of rehabilitation in Geriatric Day Hospital (GDH), he can achieve complete functional independence
  – Walking unaided
  – Modified Barthel Index 89/100 $\rightarrow$ 100/100
Discussion:

SUMMARY

What Have I Learned from My Patient?
Discussion:

**COMPLEXITY**

**INSTABILITY / SYNCOPE**

Dizziness → Syncope

**Intrinsic Factors:**
- Hearing impairment
- Co-existing diseases:
  - Arrhythmia: slow atrial fibrillation
  - Right middle ear pathology
- Concurrent illness:
  - Upper respiratory infection (URI)

**Extrinsic Factors:**
- Digoxin overdose
- Post-RAI hypothyroidism
- Side effects of flu medications (piriton, cocillana)

**IATROGENESIS**

- Painkillers (e.g. NSAIDs)

**Left Knee Injury and Patellar Fracture**

**Functional & Social Impairment**
Discussion:

What Have I Learned from My Patient?

• Drugs & Elderly
  – Age-related changes in pharmacokinetics
  – High index of suspicion in drug toxicity in elderly
  – No single geriatric dose
  – Individualized dosing method based on:
    • Body build (lean body mass, adipose tissue)
    • Renal function
    • Concomitant diseases
    • Drugs (polypharmacy)
  – Start low and go slow
  – Lower & narrower therapeutic range of digoxin
Comment

End of Presentation
Discussion:

Should we use Digoxin in this Patient?

• Indications of Digoxin:
  (AHA/ACC Guideline 2005)
  1. Heart failure

  Persistent symptoms in patients with systolic heart failure (LVEF <45% & sinus rhythm) despite optimal therapy with ACEI, beta-blocker & diuretics (Class IIa)

ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult. Circulation 2005;112;e154-e235
Discussion:

Should we use Digoxin in this Patient?

• Indications of Digoxin:
  (AHA/ACC/ESC Guideline 2006)

  2. Atrial fibrillation with rapid ventricular response
  Intravenous administration of digoxin in patients with AF & heart failure who do not have an accessory pathway. *(Class I Level B)*
  Digoxin effective to control heart rate at rest in patients with AF & indicated for patients with heart failure, LV dysfunction, or for sedentary individuals *(Class I Level C)*
  A combination of digoxin & either a beta blocker / non-dihydropyridine calcium channel antagonist is reasonable to control the heart rate both at rest and during exercise in patients with AF. *(Class IIa Level B)*

*ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation.*
What Should We Do?

1. Stop digoxin
2. Reduce the dose of digoxin
3. Stop digoxin and change to other rate limiting agents e.g. beta-blocker
4. Give digoxin immune Fab
Discussion:

What Should We Do?

1. Stop digoxin

2. Reduce the dose of digoxin to 62.5 microg daily instead of 125 microg daily

3. Stop digoxin and change to other rate limiting agents e.g. beta-blocker

4. Give digoxin immune Fab
Discussion:

Mr TC Shum 83/M

MULTI-DISCIPLINARY MULTIFACTORIAL GERIATRIC ASSESSMENT & INTERVENTION

Dizziness → Syncope → Fall
- Advanced age
- Hearing impairment, right middle ear pathology
- Slow atrial fibrillation, digoxin overdose, post-RAI hypothyroidism
- Upper respiratory infection (URI), anti-cholinergic effect of anti-histamine

Left Knee Injury and Patellar Fracture

ENT Surgeon

Orthopedic Surgeon

Physician/Geriatrician

Functional & Social Impairment

Disease treatment
Syncope & Fall Assessment & Intervention
In-Patient (Ward) & Out-Patient (GDH) Geriatric Rehabilitation

Functional Independence & Social Activities

Nurse
Physiotherapist
Occupational Therapist
P&O
Discussion:

What Have I Learned from My Patient?

- Application of **Evidence-Based Medicine** to day-to-day practice
  - Lower & narrower therapeutic range of digoxin
  - Nomogram for dose determination aids clinical decision
Fall Assessment of this Patient

- Age over 80 years
- Fear of falls
- History of previous falls
- Acute illness
- Chronic illness
- Osteoporosis
- Cognitive impairment
- Impaired strength & balance
- Hearing & visual impairment
- Urinary/bowel, incontinence, urgency and frequency
- Poor nutrition & poor hydration
- Polypharmacy & types of drugs
- Physical restraints
- Environmental hazards
- Clothing & footwear (inappropriate, no support / ill-fitting)

Fall Assessment of this Patient

- **Intrinsic Factors:**
  - Age over 80 years
  - Fear of fall
  - History of previous falls
  - Acute illness
  - Chronic illness
  - Osteoporosis, arthritis
  - Cognitive impairment
  - Impaired strength & balance, gait deficits
  - Hearing & visual impairment
  - Urinary/bowel, incontinence, urgency and frequency
  - Poor nutrition & poor hydration

Fall Assessment of this Patient

- **Extrinsic Factors:**
  - Living alone, impaired activities of daily living
  - Use of assistive devices
  - Polypharmacy & high risk medications
  - Environmental hazards
  - Clothing & footwear (inappropriate, no support / ill-fitting)

Impression

In this patient who have a change in the clinical status while taking relatively high dose of digoxin but no apparent evidence on ECG for toxicity.

*Clinical pharmacology and physiology conference: Digoxin toxicity in the elderly*  
Mr TC Shum

• Medications:
  – Aspirin 80mg OM
  – Digoxin 187.5 microgram daily
  – Pepcidine 20mg BD
What are the Differential Diagnoses in this Patient?

<table>
<thead>
<tr>
<th>Category</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>Arrhythmia: brady/tachy-arrhythmia</td>
</tr>
<tr>
<td></td>
<td>Structural heart problem</td>
</tr>
<tr>
<td></td>
<td>Acute coronary syndrome</td>
</tr>
<tr>
<td>Neurological</td>
<td>Transient ischemia attack of brainstem (vertebrobasilar insufficiency)</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td>Neurally mediated</td>
<td>Situational syncope (cough)</td>
</tr>
<tr>
<td>Drug-induced</td>
<td>Digoxin toxicity</td>
</tr>
<tr>
<td></td>
<td>Anti-cholinergic effect of anti-histamine</td>
</tr>
</tbody>
</table>
**Renal Function**

**Discussion:**

<table>
<thead>
<tr>
<th>Antihypertensive and Cardiovascular Agents</th>
<th>Normal Dosage</th>
<th>% of Renal Excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>0.125 mg every other day/every day</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>0.25 mg by mouth every day</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dosage Adjustment in Renal Failure</th>
<th>GFR &gt;50</th>
<th>GFR 10–50</th>
<th>GFR &lt;10</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>None</td>
<td>None</td>
<td>Dose for GFR 10–50</td>
<td></td>
</tr>
<tr>
<td>CAPD</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>VVH</td>
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</tbody>
</table>

doi:10.1016/j.cger.2009.04.004
Discussion:

Effects of Digoxin

• Hemodynamic Effects
  – Inhibits Na\(^+\)-K\(^+\) ATPase $\rightarrow \uparrow$ intracellular Na $\rightarrow \uparrow$ intracellular Ca via Na\(^+\)-Ca\(^{2+}\) exchanger $\rightarrow \uparrow$ systolic contraction

• Neurohormonal Effects
  – Affects sensing of changes in arterial pressure
  – ↓ Level of neurohormones (circulating nor-adrenaline)
  – ↓ Sympathetic Effect
  – ↑ Parasympathetic Activity

• Electrophysiological Effects
  – ↓ SA node pacemaking via ↑ vagal tone
  – ↓ AV node conduction
Discussion:

Rising Mortality with Increasing Serum Digoxin Concentration (SDC)

AF

CHF
CT Temporal Bone (Plain)

- Soft tissue lesion in right middle ear cavity with bony erosion involving middle ear ossicles, scutum, bony wall of facial nerve canal, and possibly infero-lateral wall of right vestibule. It can be chronic inflammatory changes with cholesteatoma formation.

- Opaque right mastoid cells with sclerosis, suggestive of chronic inflammatory changes.