Hawke's Bay Age Related Residential Care Digoxin Monitoring Guidelines

Revised April 2018

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Acknowledgments:

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Summary

Routine therapeutic drug monitoring (TDM) during digoxin therapy is not required, including daily apical pulse assessment and digoxin serum levels. The patient's heart rate should continue to be assessed as part of the patient's routine monthly clinical assessment.

Indications for TDM during digoxin therapy include:

- Confirmation of toxicity (in the presence of symptoms of digoxin toxicity)
- Assessing the effect of factors that alter digoxin's pharmacokinetics (e.g. renal impairment, drug interactions)
- Initiating therapy or dose changes (in patients with renal impairment)
- Therapeutic failure
- Medication adherence

Signs and symptoms of Toxicity

- Common
  - Nausea, vomiting, anorexia, fatigue, confusion, dizziness
- Rare or dose dependant
  - Visual disturbances (blurred vision, green-yellow colour disturbances)
  - Cardiac arrhythmia

Therapeutic Range

- Heart failure
  - 0.6nmol/L – 1.2nmol/L,
  - Toxicity more likely >2.5nmol/L[1],
  - Small increase in mortality with concentrations >1.5nmol/L.
- Atrial Fibrillation (AF)
  - 0.6 – 2nmol/L,
  - Toxicity more likely >2.5nmol/L[1],
  - Serum digoxin levels correlate poorly with ventricular rate.
  - In patients who are symptomatic, a low digoxin level may indicate the patient could benefit from a dose increase.

Samples for digoxin TDM should be take at least six to eight hours after the last dose, or ideally immediately before the next dose.

Rate Control in AF

Recent guidance from the European Society of Cardiology (ESC), indicates lenient rate control (<110bpm) may be effective in patients who are asymptomatic.

Bradycardia (heart rate <60bpm) is poorly correlated with digoxin toxicity. Patients with heart failure presenting with bradycardia (<60bpm) who are asymptomatic can be safely given digoxin. If symptomatic bradycardia is present, or the patient displays signs and symptoms of digoxin toxicity, the prescriber should be contacted.

[1]Medsafe. Wellington: New Zealand Medicines and Medical Devices Safety Authority. Lanoxin® Data sheet. Accessed online 21/11/2017 from www.medsafe.govt.nz

Background

Digoxin is a cardiac glycoside indicated in the treatment of atrial fibrillation (AF) and heart failure (HF). Digoxin's mechanism of action is thought to be mediated through inotropic effects and neurohormonal effects[2]. Positive inotropic effects from digoxin arise from the inhibition of Na^+–K+-ATPase and secondary activation of the Na^+–Ca^{2+} membrane exchange pump resulting in increased force of cardiac contraction[2]. Neurohormonal effects mediate increased vagal tone, decreased sympathetic tone, leading to prolonged refractory period and slowing of conduction through the atrioventricular node, thereby slowing ventricular rate[2]. Neurohormonal effects are present at lower digoxin serum levels and are considered primarily responsible for the therapeutic actions in both heart failure and atrial fibrillation[33] Inotropic effects are present at higher digoxin serum levels and are now considered less important in the therapeutic effects of digoxin[3].

Heart Failure

The European Society of Cardiology 2016 Heart Failure guidelines recommend digoxin to be considered in patients[4] with heart failure and sinus rhythm where patients remain symptomatic despite treatment with an ACE-Inhibitor, β-blocker, diuretics and spironolactone[4]. Conflicting evidence exists on the use of digoxin in patients with heart failure and AF, with a recent randomised study showing deterioration in HF when digoxin is used for rate control compared with a meta-analysis of non-randomised trials suggesting no negative effects[4]. The ESC guidelines recommend digoxin in patients with AF and heart failure if other options are not tolerated or contraindicated[4].

Atrial Fibrillation

Digoxin slows resting ventricular heart rate in patients with chronic atrial fibrillation. Digoxin is less effective at controlling exercise or stress induced atrial fibrillation. It can be successfully used in combination with β-blockers, verapamil and diltiazem for the management of chronic atrial fibrillation[5].

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[2] Auman J, DiDemenico R, Galanter W. Mechanisms, Manifestations and Management of Digoxin Toxicity in the Modern Era. Am J Cardiovasc Drugs. 2006; 6: 77-86

[3] Barclay M, Begg E. The practice of digoxin therapeutic drug monitoring. NZMJ. 2003;116(1187)

[4] Piotr Ponikowski, Adriaan A. Voors, , Stefan D. Anker, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). European Heart Journal. 2016; 37: 2129–2200

[5] Campbell T, MacDonald P. New Drugs, Old Drugs: Digoxin in heart failure and cardiac arrhythmias. MJA. 2003; 179: 98-102

Requirements for Apical Pulse Monitoring

Conflicting information exists in the literature as to whether apical pulse (see Appendix 3 for further information on apical pulse) monitoring is required before the administration of digoxin. Current NZGG atrial fibrillation[6] and congestive heart failure[4] guidelines do not require apical pulse monitoring, nor does the data sheet for Lanoxin® brand of digoxin[1].

The BNF[7] and MICROMEDEX[8] suggest apical pulse assessment prior to the administration of digoxin, with each giving an apical pulse < 60 beats-per-minute (bpm) as a point in which the either patient or caregiver should contact the prescriber before administering digoxin.

The basis to this advice is that the presence of bradycardia may indicate digoxin toxicity or heart block[9]. An early study correlating heart rate and digoxin toxicity found that sinus bradycardia or slow ventricular rate was poorly correlated with digoxin toxicity (6 out of 57 patients)[10]. A later study found that digoxin was inappropriately withheld in 81% of patients with a heart rate of < 60bpm[9].

The incidence of digoxin toxicity is considerably lower than that observed in early studies. Studies from the 1970s indicated 25% of patients on digoxin experienced toxicity, reducing to 4% with the DIG trial during 2000s[2]. The advent of therapeutic drug monitoring standardised digoxin formulations and reduced target therapeutic ranges has reduced the rate of toxicity. Renal impairment is one the most important risk factors, with moderate renal impairment being present in 66% of toxicity cases[2].

Patients with AF have a rhythm, which is defined as “irregularly irregular”. In overdose and severe digoxin toxicity heart block can develop, leading to sinus (regular rhythm) bradycardia of between 45 – 60bpm. Heart block can also occur with the combination of other AV node blocking agents e.g. β-blockers and calcium channel blockers. Other arrhythmia likely in digoxin toxicity include premature ventricular complexes and sustained ventricular tachycardia[2].

Patients with bradycardia should be assessed for other clinical signs and symptoms. It is unlikely that a patient will be symptomatic of bradycardia if their apical pulse is >50bpm. Patients presenting with hypotension, syncope, chest pain, and shortness of breath along with bradycardia should be assessed by their doctor[11].

Recommendations:

Assess blood pressure and apical pulse as part of the patient’s routine monthly clinical assessment

See Appendix 1: Aged Residential Care digoxin monitoring wall chart

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[6] New Zealand Guidelines Group. New Zealand Cardiovascular guideline handbook. Atrial Fibrillation and Atrial Flutter: Assessment and therapy. Ministry of Health. Wellington, New Zealand. 2005.

[7] Joint Formulary Committee. British National Formulary. 72nd ed. London: British Medical Association and Royal Pharmaceutical Society; 2016

[8] Micromedex® Healthcare Series. Drugdex Evaluations: Digoxin. Thomson Reuters (Healthcare) Inc. Accessed online 30/9/11 from http://www.thomsonhc.com

[9] Walthall S, Odtoham B, McCoy M, Fromm B, Frankovich D, Lehmann M. Routine withholding of digitalis for heart rate below 60 beats per minute: Widespread nursing misconceptions. Heart Lung. 1993; 22:472-6.

[10] Williams P, Aronson J, Sleight P. Is a Slow Pulse a Reliable Sign of Digitalis Toxicity?. Lancet. 1978 Dec 23: 1340-42.

[11] Livingston M; Brown D Sinus Bradycardia. Accessed online 21/11/17 from http://emedicine.medscape.com/article/760220-overview

Signs and Symptom of toxicity

Digoxin toxicity can present as gastrointestinal symptoms, cardiac symptoms and neurological symptoms.

Gastrointestinal[2] (most likely)

- Nausea
- Vomiting
- Anorexia

Neurological[2]

- Weakness
- Fatigue (most likely)
- Dizziness
- Confusion
- Visual disturbance
    - Blurred vision, flashing lights or halo's
    - Green-yellow colour disturbances

Cardiac[2]

- Supra ventricular arrhythmia
- Ventricular arrhythmia
- First, second or third degree heart block
    - Sinus Bradycardia
- Tachyarrhythmia's are more common in patients with heart disease

Documentation for reporting signs and symptoms of toxicity

Many of the symptoms of digoxin toxicity (nausea, confusion, arrhythmia, and abdominal pain) are non-specific and are frequently present in acutely ill patients in general.

Suspected digoxin toxicity should be documented in the patient's progress/medical notes, and the following information sent to the patient's GP using the facility or digoxin ISABR (see Appendix 4):

- **Observations**
    - Blood pressure
    - Heart rate
    - Alterations in food intake
    - Neurological status
- **Signs of toxicity**
    - Gastrointestinal
    - Visual
    - Neurological

Monitoring Requirements for Digoxin Therapy

Therapeutic range:

- HF 0.6 – 1.2nmol/L[3]
- AF 0.6 – 2nmol/L[12]* (see notes below)

Digoxin therapy for HF symptoms has been shown to be effective at lower concentrations (0.6 to 1.2 nmol/L)[2]. Therapy in lower concentrations was associated with a small but significant reduction in all-cause mortality, worsening heart failure, all-cause hospitalisation and hospitalisation due to heart failure compared with placebo[5]. Higher concentrations (>1.5nmol/L) were associated with a small but significant increase in all-cause mortality, cardiovascular mortality and hospitalisation for digoxin-related toxicity. Mid-range was not significantly different from placebo for toxicity[2].

Studies evaluating the relationship of serum digoxin concentrations with pharmacodynamic effects in AF have in general, shown a poor correlation between digoxin levels and ventricular rate. This is understandable, considering the many other factors that affect conduction through the AV node[14]. The ventricular rate, although a clinically important and easily monitored parameter in AF, may not always be a good measure of digoxin effect[5]. In some patients, signs and symptoms of toxicity may develop before the desired decrease in heart rate[2]. The serum digoxin level may provide information that cannot be obtained solely from the clinical picture, but is of great relevance to therapeutic decision making[12].

The indications for digoxin TDM are relatively few and include confirmation of clinically suspected toxicity, assessing the reasons for therapeutic failure, assessing medication adherence, and assessing the effects of factors that alter the pharmacokinetics of digoxin (predominantly renal dysfunction and drug interactions). The clinical suspicion of toxicity correlates poorly with high digoxin concentrations. In those requests in which the indication for TDM was confirmation of toxicity, only 19% were associated with a high digoxin concentration[13].

Samples for digoxin TDM are required to be taken at least eight hours after the last dose or ideally immediately before the next dose. This allows for the redistribution of digoxin from plasma into the tissues. It is ideal that digoxin levels are taken when concentrations are at steady state. The relatively long half-life of digoxin (30 hours in patients with normal renal function) means that following initiation or dose alterations, it takes at least 7 days for steady-state concentrations to be achieved. In the elderly with impaired renal function the half-life can be extended to 3.5-5days, meaning 14-20days may be required before steady state is acheived[2].

Recommendations:

See Appendix 2: Monitoring requirements for digoxin wall chart.
See Appendix 4 is a suggested format for recording monthly blood pressure and apical, along with routine assessments of eGFR and potassium.

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[12] Masuhara J, Lalonde R. Serum digoxin concentrations in atrial fibrillation: a review. Ann Pharmacother. 1982; 16:543-546

[13] Sidwell AI, Barclay ML, Begg EJ, Moore GA. Digoxin therapeutic drug monitoring: an audit and review. NZ Med J 2003;116(1187)

Actions on Therapeutic Level

Serum digoxin levels should be interpreted within the clinical context. If the level is above the therapeutic range, the dose should be reduced even if toxicity is not observed. This is based on the observation that the patient is at risk of arrhythmia, and no further clinical benefit is likely with higher concentrations. Toxicity is observed when digoxin levels are within the normal range, due to other factors, which alter tissue sensitivity to digoxin, for example[3]:

- Hypokalaemia (low potassium)
- Hypercalcaemia (high calcium)
- Hypothyroidism (thyroid disease resulting in reduced thyroid function)
- Hypoxia / acidosis (low blood oxygen, arterial blood pH <7.35)

Digoxin TDM may be useful to detect the patients who have a low digoxin concentration and who may benefit from an increase in digoxin dose, as opposed to those with higher concentrations who are likely to develop toxicity symptoms only from an increase in dose[13].

Recommendations:

See Appendix 2: Monitoring requirements for digoxin wall chart

Medication Interactions

Digoxin is rapidly absorbed with a bioavailability of 70-80% from oral tablets. Digoxin is eliminated primarily by renal excretion, via P-glycoprotein (P-gp). Interactions with digoxin are mediated through the inhibition or induction of P-gp in the GI tract and renally. Inhibition of renally located P-gp results in increased serum digoxin levels. Induction of P-gp in the gut reduces digoxin absorption, resulting in lower levels[14].

Medications that increase the risk of toxicity[14]

- Reduce the dose of digoxin prior to initiating therapy:
    - Amiodarone (50% dose reduction when initiating amiodarone)
    - Verapamil (50% dose reduction when initiating verapamil)
- Monitor digoxin level (7 days-21 days depending on renal function after introducing the interacting medicine)
    - Clarithyromycin / erythromycin / roxithromycin
    - Spironolactone
    - Cyclosporin
    - Itraconazole
    - Diltiazem
    - Quinine
    - Atorvastatin (high doses only 80mg daily)
    - Trimethoprim (courses >7 days)
- Monitor renal function and potassium level (every 3-6 months or after vomiting, diarrhoea or dehydration)
    - Diuretics (risk of hypokalaemia)
    - ACE-Inhibitors (reduction in renal function – monitor 7 days after starting then 3-6 monthly)

Medications that decrease digoxin levels[14]

- Decreased absorption (Monitor Levels 7-21 days after introducing the interacting medicine)
    - Rifampicin
    - St John's Wort
- Decreased absorption (separate administration by 2 hours)
    - Antacids (aluminium and magnesium, not calcium based)

Recommendations:

See Appendix 2: Monitoring requirements for digoxin wall chart

[14] Hanratty C, McGlinchy P, Johnston D, Passmore A. Differential Pharmacokinetics of Digoxin in Elderly Patients. Drugs Aging. 2000;17:353-62

Medical conditions increasing the risk of toxicity

In the elderly reduced renal function and a reduction in muscle mass (20% between 20 and 70 years), increases serum digoxin levels and reduces elimination of digoxin[14]. The following changes in medical conditions can increase the risk of digoxin toxicity either due to increased digoxin concentrations or sensitivity to digoxin[2].

- Dehydration – nausea and vomiting
- Renal impairment
- Unstable heart failure
- Hypokalaemia – over diuresis
- Hypothyroidism
- Myocardial Infarction
- Hypercalcaemia

If signs or symptoms of digoxin toxicity present, TDM is indicated.

Quality Improvement (QI) activity

The presence of this guideline locally provides a great QI activity in any ARRC facility in Hawke's Bay. Consider reviewing all patients who are on digoxin in your facility as a quality improvement activity/audit. This can be done annually. Below are some guidance to aid with the audit.

The audit should include the following categories:

- Aim: *what is the purpose of the audit*
- Measurement: *e.g. reviewing documentation of monitoring parameters (see appendix 5) for each patient on digoxin in the facility over a year period*
- Results: *feedback to the team the results, what was done well and areas of improvement*
- Action: *work on areas of improvement as necessary and when to re-audit if necessary*

Audit Template

Please note this is a basic template that you may choose to utilise for quality improvement audit.
Please ensure that the audit is applicable to your practice.

TOPIC	**Topic: Digoxin monitoring in Age Related Residential Care** **Why is this topic of interest?** Digoxin has a narrow therapeutic index and its levels are affected by declining renal function hence monitoring patients on digoxin is essential for safe and effective use. **Recommended readings:** - Hawke's Bay's Aged Related Residential Care Digoxin Monitoring Guidelines
PLAN	**Indicators** The nursing staff undertake a review of digoxin monitoring for patients on digoxin in the facility. Local guideline outlines minimum standard of digoxin monitoring for patients. **Criteria (how will the indicator be measured)** The aim of this audit is to ensure adherence to standards outlined in Hawke's Bay's Aged Residential Care Digoxin Monitoring Guidelines. The following areas to be audited: - Presence of digoxin monitoring chart- Yes= Pass and No= Not passed - Required monitoring frequency for the patient documented- Yes= Pass and No= Not passed - Baseline monitoring data for the patient documented- Yes= Pass and No= Not passed - Monitoring documented for the specified frequency (3, 6 or 12 monthly)- Yes= Pass and No= Not passed **Standards (the standards to be achieved)** The focus of this project is on improving standards of clinical practice hence an acceptable target is that all patients meet the guideline standards.
DO	**Discover what you are doing now (collect data)** Use the tool provided to conduct your activity. Please note this is a basic template you may choose to alter or change the document as appropriate for your facility to ensure safe and effective use of digoxin.

STUDY	**Analyse what the results tell you** Analyse your results using the data sheet on the next pages. Consider the following: a. Does your data appear complete? Consider the documentation b. What part of digoxin monitoring requires the most improvement? c. Did the audit identify things that were done well? What were they? d. Did the audit find areas of improvement?
ACT	**Make changes – what changes can be made to improve patient care?** • Based on your facility's results, what monitoring standards are not adhered to? • What can you do to support better adherence? • Plan and implement education or other means to support adherence to the guidelines. This should be done within 3 months of audit findings. • Plan a review date to follow up on changes.

Quality Improvement Activity

Topic: Digoxin monitoring in Age Related Residential Care Facility audit

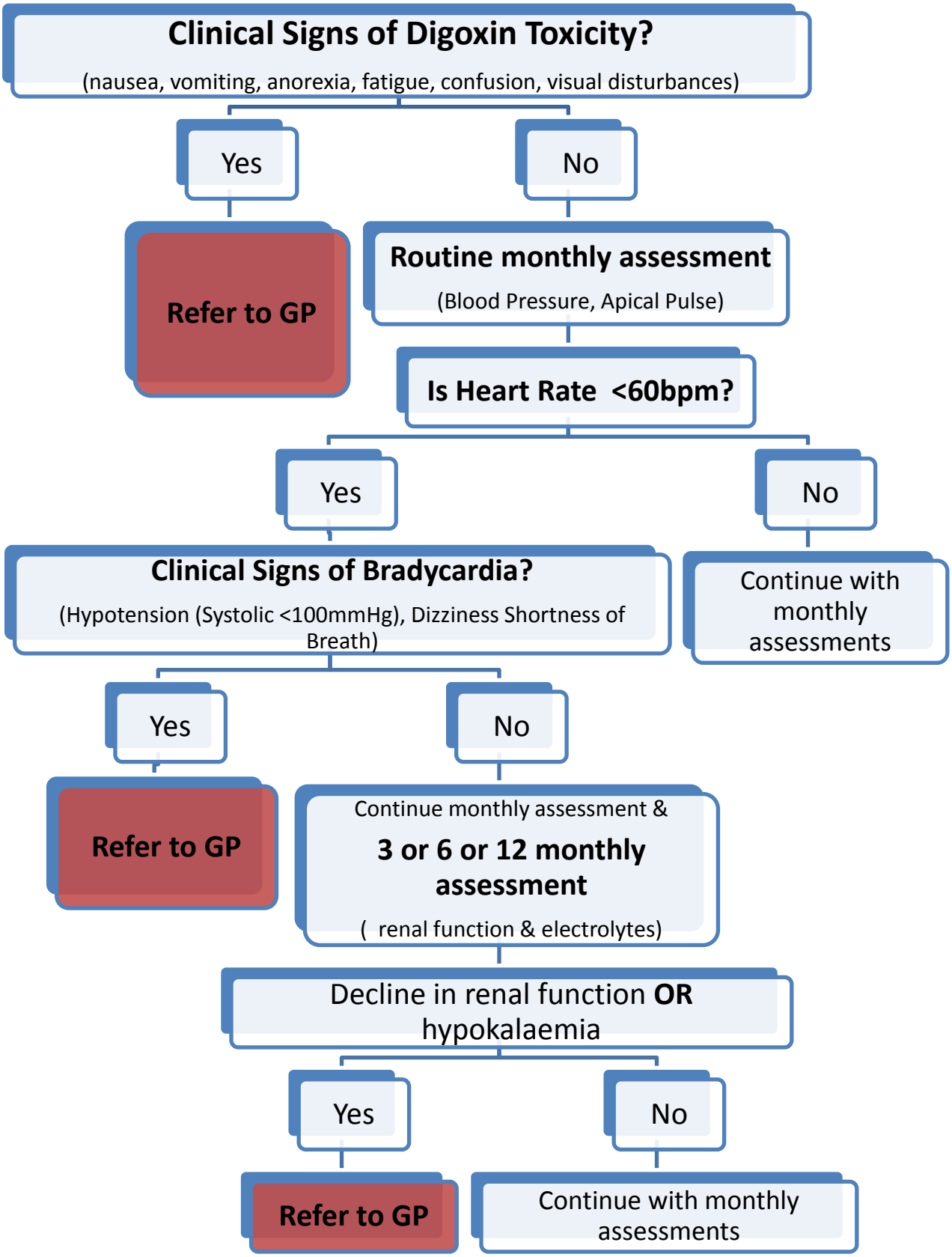
Facility name: _____ Date of collection: _____

Sample size: identify all patients in your facility on digoxin, you can do a manual check of all the medication charts the patients are on (this could be paper based or Medimap etc. The community pharmacy that supplies the medications to your facility may be able to identify patients in your facility that are on digoxin.

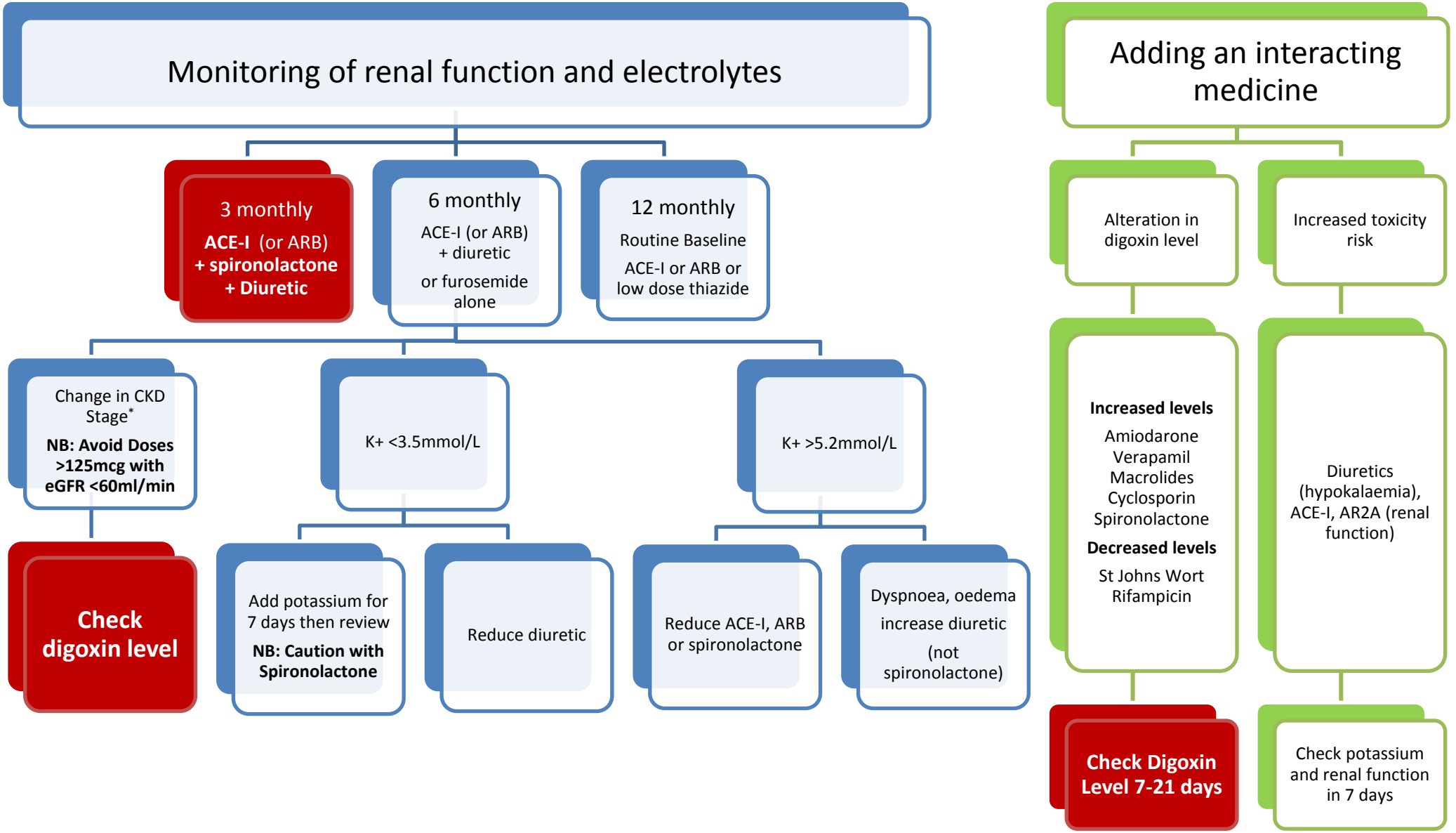
Patient	Does the patient have a digoxin-monitoring chart attached to their monitoring chart? (Y or N)	Does the patient have monitoring frequency documented on their digoxin-monitoring chart? (Y or N)	Are baseline data provided (tick where applicable)	Was the monitoring as per specified frequency? (Y or N)	This patient monitoring passed? (Y or N)
			BP and apical rate ☑ eGFR ☐ Potassium ☐		
			BP and apical rate ☐ eGFR ☐ Potassium ☐		
			BP and apical rate ☐ eGFR ☐ Potassium ☐		
			BP and apical rate ☐ eGFR ☐ Potassium ☐		
			BP and apical rate ☐ eGFR ☐ Potassium ☐		

Check: Describe any areas targeted for improvement as a result of analysing the data collected.
Action: Describe how these improvements will be implemented.
Monitor: Describe how well the process is working.
Comments:

Appendix 1. Residential Care Digoxin Monitoring Wall Chart



Appendix 2. Monitoring requirements during digoxin therapy wall chart



Appendix 3. Guideline for Residential Care: Taking an apical (apex) beat

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GUIDELINE FOR RESIDENTIAL CARE

TAKING AN APICAL (APEX) BEAT

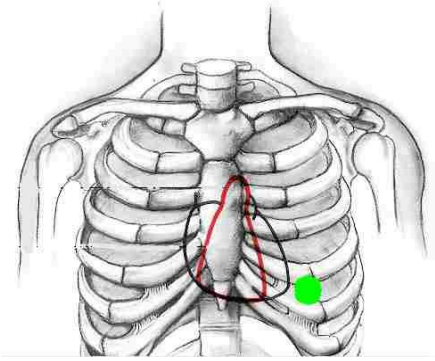
Definition

The Apical (Apex) beat is the heart beat of the heart. The heart beats with two distinct sounds (lub-dub). Each set of sounds (lub-dub) is one heartbeat. The Apical (Apex) Pulse is counted for a full minute denoting rate, rhythm and volume

Good Practice: Any resident who is prescribed Digoxin is to have a monthly Apical (Apex) Pulse recorded and documented.

To assess

1. Provide resident privacy
2. Assist the resident to sit up or assume a semi-sitting position
3. Expose the resident's chest
4. Examine the chest to find the anatomical landmarks for proper stethoscope placement.



5. First locate the first intercostal space (the space between the first and second rib) on the left side of the chest.
6. Count down to the fifth intercostal space (between the fifth and sixth rib).
7. Draw a straight line from the left nipple to the fifth intercostal space (or landmark by drawing a line from mid clavicular) to identify the area of the apical pulse.
8. Use your hand to warm the stethoscope diaphragm, (the flat disk) side of the stethoscope.
9. Listen and count for the heart beat for 60 seconds.
10. The heart beat consists of two distinct sounds, lub-dub.
11. Each lub-dub counts as one heartbeat.
12. Please report (refer to ISBAR communication tool to GP) if you denote the following:

The heart beat is not regular/missing a beat	The heart beat is weak or bounding
Nausea (length of time)	Vomiting (length of time)
Anorexia (length of time)	Fatigue (describe)
Chest pain (describe)	Confusion (new/old)
Dizziness (rule out postural drop)	Shortness of breath (new/length of time)

13. Don't forget to document your findings.

Appendix 4: Digoxin ISBAR

COMMUNICATION TOOL **DIGOXIN COMMUNICATION**

TO GENERAL PRACTITONERFROM AGED RESIDENTIAL CARE

I

To Dr: ……From: (Facility) ……

(Fax number of Facility)……..

Resident's Name: ……Residents NHI: ……..Residents DOB: ……

Staff member: (Name and role) ……

I am calling because I perceive there are concerns relating to the patients prescribed medication and side effects – Medication = Digoxin

S I believe this resident is *(tick indicates concerns)*

☐ Stable but I have concerns ☐ Unstable with rapid/slow deterioration

B Has been prescribed Digoxin *(tick indicates concerns)*

☐ Long- term medication (months to year) ☐ Recently prescribed by yourself

☐ Recently prescribed from a Hospital discharge ☐ Unclear of when it was prescribed

A **I have taken the residents Apical Pulse and it is <60 beats per minute, along with symptoms of bradycardia (hypotension, chest pain, syncope, and SOB) – <u>this is new from last taken</u>**

The resident is complaining/displaying:

☐ Nausea (length of time) ☐ Vomiting (length of time)
☐ Anorexia (length of time) ☐ Fatigue (describe)
☐ Chest pain (describe) ☐ Confusion (new/old)
☐ Dizziness (rule out postural drop) ☐ Shortness of breath (new/length of time)

If you have ticked any of the boxes above the RN to please document your findings:

……

……

Apical Pulse (Reg/quality): ……(this is different from last assessment on ……/……/…….)

Other Vital signs completed:

Temp:…….. BP (L & S)……-Resps:……Oxygen Sats:….

Any changes

Skin colour Y/N Pain Y/N Urine output Y/N Bowel changes Y/N

R Please confirm advice on further management:

……..

☐ **Digoxin ISBAR sent**
☐ General Practice responded

Appendix 5. Digoxin Monitoring Chart- PLEASE FILE WITH MEDICINE CHART

Patient Details: Attach Sticker
Name:
NHI:
Doctor:

Monitoring Frequency
BP and Apical Pulse:
eGFR:
Potassium:

Date	Apical Pulse	BP	eGFR *3, 6 or 12 monthly depending on Appendix 2*	Potassium (K+) *3, 6 or 12 monthly depending on Appendix 2*

Please refer to Digoxin Administration Monitoring Wall Charts and Guideline for further information.