Sterile Preparation of I-131 Solution

For Feline Hyperthyroidism

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Learning Objectives

1. Describe the treatments available for feline hyperthyroidism
2. Identify the methods of administration of I-131 solution for feline hyperthyroidism
3. Discuss the method of preparation and the effect of filter size when preparing the sterile solution
4. Discuss the I-131 filtering protocol and bubble integrity testing
5. Describe the anticipated effect of the pH of the final preparation
6. Identify the diluents and their effect on the final preparation
7. Apply the principles of radiation safety

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Assessment question 1

What are the available treatments for feline hyperthyroidism?

a. Methimazole
b. Surgery
c. Radioiodine (NaI131)
d. Iodine restricted diet
e. All of the above

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Assessment question 2

Which treatment is the most preferred for feline hyperthyroidism?

a. Methimazole
b. Surgery
c. Radioiodine (NaI131)
d. Iodine restricted diet

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Assessment question 3

Which is an advantage of using NaI131 over medical and surgical treatment for feline hyperthyroidism?

a. Has harmful side effects
b. Causes destruction of healthy tissue
c. Causes hypoparathyroidism
d. Eliminates the need for anesthesia

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Background

Radioiodine has been clinically used in the treatment of hyperthyroidism and cancer treatment of the thyroid since 1941

Typically, available for oral administration in outpatient settings

Commercially available product / no information regarding pyrogenicity or sterility

Radioiodine is also used to treat feline hyperthyroidism – most common endocrine disorder in the feline population

Feline hyperthyroidism is a disorder of the endocrine system manifested in cats older than 10 years of age.

The disorder is difficult to diagnose due to symptoms that may mimic several other conditions

Eliminates the need for anesthesia and risk of hypoparathyroidism

Sodium iodide is a water- soluble ionic compound used as a diagnostic agent for the evaluation of thyroid function.

Oral solution contains: 0.05N NaOH and 0.02N Sodium thiosulfate pentahydrate, and up to 40mg of dibasic sodium phosphate (as stabilizers)

pH of the oral solution: 7.5 to 10

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Available treatments for feline hyperthyroidism

Medicine

- Methimazole: thioamide
- inhibits synthesis of thyroid hormones by two process
1. Block oxidation of iodine in the thyroid gland
2. Blocks synthesis of thyroxine and triiodothyronine (T3)
- circulating T4 and T3 – not inactivated

Radioactive iodine

- Sodium Iodide – I131
- Rapidly absorbed in the bloodstream and distributed w/in the diseased thyroid tissue
- Once in the thyroid – overactive portions of the thyroid is destroyed.
- Post thyroid concentration – get oxidized to iodine
- Thyroid tissue is destroyed by beta emission

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Available treatments for feline hyperthyroidism

Surgery

- Requires anesthesia
- May need to be repeated
- May cause deficiency of the parathyroid hormone
- May not be as effective in removing the affected tissue of the condition.

Iodine restricted Diet

- Not curative
- Lower rate in controlling the disease state
- May be more difficult to monitor

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Assessment question 4

How long should methimazole be discontinued prior to the administration of NaI-131 treatment?

a. 1 day
b. 3 days
c. 5 days
d. 7 days

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Methimazole vs Radioactive iodine

Methimazole

- Absorption: almost complete
- Distribution: mostly concentrated in thyroid gland
- Metabolism: hepatic; takes 1-2 hours to peak in serum w/36-72 hours duration of action
- Excretion: urine
- Daily administration

Radioiodine 131

- Absorption: (oral) rapid - 90% within 60minutes of administration
- Distribution: extracellular space; primarily trapped by the thyroid
- Metabolism: iodide → metabolized to iodine in the thyroid
- Excretion: Urine; feces
- Treatment may be repeated one more time (if needed)

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Assessment question 5

The preferred method of administration of NaI131 solution for treatment of feline hyperthyroidism is:

a. Transdermal gel
b. Orally
c. Enema solution
d. Subcutaneous

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Methods of Administration of I-131 solution

- Oral / transdermal gel
- Enema solution
- IV administration
- Subcutaneous (preferred route)

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Method of preparation of sterile NaI-131 solution and effect of filter

Items needed:

- Stock solution of NaI-131
- Filter: several types available – more details on next slides
- Sterile water for injection – used to QS I-131 solution prior to filtration (SWFI has neutral pH – 7 and can vary from between 6.5 – 8.5)
- 0.9% Sodium Chloride (0.9%NaCl) - has a pH – around 5.5
- 1 x TB syringe
- 1 x 3cc syringe w/25G needle for final dispensing

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Assessment question 6

Which filter provides the least volatility post NaI131 filtration?

a. Millex-GP 0.22um 13mm
b. Millex-LG 0.20um 25mm
c. Millex-GV 0.22um 33mm
d. Millex-GV 0.22um 13mm

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Filter type

Filter	Size	Millipore product number	Type
Millex-GP 0.22	33 mm	SLGP033RS	Express polyethersulfone membrane (PES)
Millex-GV 0.22	33 mm	SLGV033RS	Low protein binding durapore (PVDF)
Millex-LG 0.2	25 mm	SLLG025SS	Hydrophilic fluoropore membrane (PTFE)
Millex-GV 0.22	13 mm	SLGV013SL	Low protein binding durapore (PVDF)

Table 1– courtesy of The University of Oklahoma

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Descriptive statistics for residual and volatility among each filter

	N	Mean	Standard deviation	Median	Lower quartile	Upper quartile
13 mm						
Net filter activity (uCi)	4	7.77	2.69	7.80	5.45	10.10
% filter activity	4	0.09	0.01	0.08	0.08	0.09
Net volatility of filter (nCi)	4	1.37	1.15	0.97	0.68	2.06
25 mm						
Net filter activity (uCi)	3	13.40	2.29	14.30	10.80	15.10
% filter activity	3	0.12	0.01	0.12	0.11	0.13
Net volatility of filter (nCi)	3	0.69	0.28	0.60	0.46	1.00
GP 33 mm						
Net filter activity (uCi)	6	18.33	3.39	19.00	15.00	20.00
% filter activity	6	0.15	0.01	0.15	0.14	0.16
Net volatility of filter (nCi)	6	29.41	65.67	1.89	1.61	6.83
GV 33 mm						
Net filter activity (uCi)	3	15.47	1.36	15.00	14.40	17.00
% filter activity	3	0.15	0.02	0.14	0.13	0.16
Net volatility of filter (nCi)	3	1.74	0.26	1.84	1.45	1.94

Table 2 - courtesy of the University of Oklahoma

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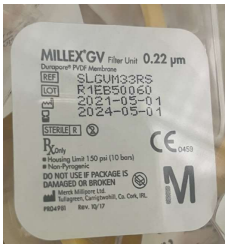
Role of filter and size
Several filters can be used for sterilization



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Filter size and volatility

- Statistically, ^{131}I volatility with each filter – not significant
- In a clinical sense, LG 0.2um 25mm - is the preferred filter to use in practice due to its lowest volatility characteristic
- The second best is the Millex-GV 0.22um 13mm.
- These filters were the best for volatility, but in the mid-range for residual activity.
- Activity can easily be adjusted by increasing filtered activity based on your demand.

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Assessment question 7

- What is the determining factor for the sterility of the solution for parenteral administration?
- a. radiation present in the NaI131 solution
- b. the filtering process
- c. the filter integrity test
- d. the membrane of the filter unit

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NaI-131 Filtering Protocol

- 1. Using a 3cc syringe, withdraw 1-2ml of sterile water for injection
- 2.Remove the needle and place on the side for later use
- 3. In TB syringe, withdraw the necessary amount of I-131: based on activity needed
- 4. Transfer the I-131 solution to the 3cc syringe and place TB syringe in shielded pig
- 5. Attach the filter unit (0.2um or 0.22um) to the 3cc syringe
- 6. re-attach the needle to the 3cc end of the filter
- 7. Filter the NaI-131 solution in a shielded sterile evacuated vial (10ml)
- 8. Perform the bubble integrity test – based on filter PSI (solution is deemed to be sterile if the filter integrity is within the manufacturer's range).

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Performing your Bubble Point Integrity Test post filtering of Na I-131 preparation

Equipment	Materials
Equipment Calibrated Pressure Gauge Apparatus	Suitable Container (beaker) filled with purified Water (QS as needed)
	Membrane Filter Used in Preparing the NaI-131 solution 50ml syringe x 1 Plastic Tubing
Other Materials for filter Rinse (optional)	Suitable sealed plastic container
	Lead pig and suitable vial for water transfer once test completed
	Charcoal placed in the storage plastic container
	5-10ml syringe with SWFI

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Performing the filter integrity test

Flush the filter with 5-10ml of SWFI. Collect in a 30ml evac vial (optional)

Pull back the plunger of a 50ml syringe and attach to the female luer lock connection of the Calibrated Pressure gauge apparatus

Attach the rinsed filter unit to the male luer lock connector of the pressure gauge

Once filter is secured, connect the plastic tubing to the other end of the filter

The distal end of the tubing will be immersed in the beaker filled with water

Begin the pressure integrity test by depressing the plunger of the 50ml syringe

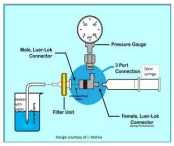
pay attention to the bubble formation in the beaker and notice the PSI reading on the Calibrated Pressure gauge

Ensure that the filter meets the indicated pressure per filter manufacturer standards. This psi number if met, will determine the sterility of the solution.

Once test completed, store and shield all materials in the fume hood for decay.

Record data on spreadsheet for future audit

Diagram of pressure gauge



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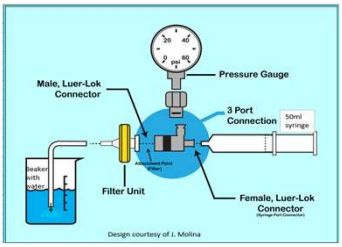

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Assessment question 8

Which diluent is most preferred by veterinarian for final NaI-131 dose injection?

a. Sterile Water for Injection (SWFI)
b. 0.9% Sodium chloride
c. Dextrose 5%-Sodium Chloride
d. Ringers Lactate

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pH effect

Blood pH – 7.35 to 7.45. Human blood: slightly basic with a pH around 7.4

Arterial blood pH – 7.4

Intracellular fluid pH – 7.0

NaI131 solution for oral administration has a pH – 7.5 to 10.0 which is basic in nature.

Commercial 0.9% Sodium Chloride (NaCl) for infusion has pH – around 5.5.

Water has a neutral pH of 7 but can vary from 6.5 and 8.5.

To maintain close level to blood pH, the hydrogen ion concentration must be balanced with 0.9% NaCl for final injection to avoid cell death or lysis.

Final solution QS with SWFI with such variable pH can remain high and is not conducive for subcutaneous injection.

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Role pH effect of final solution

- Per monograph, I-131 pH <791>
- Between 7.5 and 9 for intravenous use
- Between 7.5 and 10 for oral use.
- Subcutaneous is the preferred method for the administration of NaI-131
- The pH may be as significant when administered SC – taking into consideration the small size of the feline.
- For IV administration the pH should be within the recommended values of the monograph. However, should consider the stabilizers that are present in the solution

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Effect of Stabilizers of the NaI131 Oral solution in sterile preparation

- the study on Volatility of NaI131 solution in 2018 also focused on the final pH of the sterile solution.
- when NaI131 solution is diluted to 1 mL with 0.9%normal saline in the 3 mL syringe:
- The pH of the ^{131}I was found to be between 6.5-8.0
- Which is slightly lower than the standard range in the USP monograph of 7.5-9.0 for IV administration.
- pH range in the USP might refer to the stability of the drug without consideration for the presence of stabilizers in the commercial product.
- Presence of stabilizers such as EDTA and sodium thiosulfate can add some sodium chloride equivalence, to the manufactured product thereby rendering it to be hypotonic
- To balance the hydrogen ion and make the solution for sterile administration isotonic, the final diluent to use will be 0.9% NaCl (sodium chloride) and preferred by veterinarian.

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ALARA Principles

- Initiate the proper set up for the pre-filtering process
- Set up plastic container inside fume hood to collect items post filtering with charcoal filter
- Set up lead shield container for filter collection post filtering and bubble integrity test
- Keeping in mind the volatility of I-131 and utilizing proper ALARA principles, workers will not be placed in increased risk when preparing I-131 for parenteral administration.

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Maintaining ALARA

- Good set up prior to processing is necessary.
- Prior to filtering process of I-131, prepare a plastic bag (8x8) with charcoal filter
- Charcoal filter may be a TEDA cartridge or Mini pac
- Set up in place a lead container for 30cc or 20cc vial when performing the filter rinse
- Once filtering is completed within the fume hood, remove the I-131 embedded filter from the syringe,
- Seal the filter it in the charcoal packed plastic bag, then place in storage for decay.

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Key take aways

- Take into consideration the types of filters that can be utilized
- The proper solvent to use pre- and post-filtering ^{131}I for feline parenteral administration may be different
- Use a charcoal vented fume hood for the filtration process
- SWFI can be used as the diluent when diluting NaI131 solution for storage
- Final dilution for subcutaneous injection with 0.9%NaCl is the last step in the dispensing process, was found to be the best practice
- Oral solution, when filtered can safely be used for parenteral treatment of hyperthyroidism with great benefit to the feline population
- Keeping in mind the volatile characteristics of ^{131}I and utilizing proper ALARA principles, workers will not be placed at increased risk when preparing ^{131}I for parenteral administration.

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Assessment question 5

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Assessment question 8

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Thank You!

- Any Questions?

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