

Non-Imaging Procedures in Nuclear Medicine

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Topics Covered:

- C¹⁴ Breath Tests.
- Vitamin B¹² Absorption Tests (Shillings Test).
- Total Blood Volume Determination:
 - Plasma Volume.
 - Red Cell Mass.
 - Red Cell Survival.
 - Splenic Sequestration.
- Thyroid Uptake.

Scope of Presentation

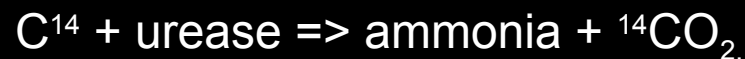
- Clinical indications.
- Radiopharmaceuticals.
- Patient preparation and procedure.
- Pitfalls and sources of error.

Carbon-14 Breath Test - Overview

- H. pylori bacteria is present in almost all patients with peptic ulcers and chronic gastritis.
- Not all patients with H. pylori will develop ulcers; however, most patients with ulcers have H. pylori overgrowth present.
- Antibiotic therapy reduces recurrence to less than 10%, while conventional drug therapy will suffer recurrence rate of 60-90% within 1st year.
- Initial diagnoses AND post treatment follow-up are common indications for C¹⁴ breath test studies.
- 96% accurate and 96% specific.

Carbon-14 Breath Test - Mechanism

- H. pylori releases *urease* (enzyme) into stomach cavity.
- Urease in stomach exists only in presence of H. pylori.
- C¹⁴ urea administered orally, then hydrolyzed into ammonia and ¹⁴CO₂ which is exhaled by lungs.
- Presence of radioactive ¹⁴CO₂ in patients breath indicates presence of H. pylori infection in patient's stomach.



(Only occurs in presence of H.pylori).

Carbon-14 Breath Test – Patient Preparation

- Follow-up studies should be performed at least 4 weeks post antibiotic therapy.
- Patient not on bismuth based compounds for at least 30 days. (*Peptobismol*).
- Off proton pump inhibitors for at least 2 weeks prior to study. (*Prilosec, Prevacid, Zantac*).
- Relevant medical history and current medication list must be obtained.
- Patient NPO for at least 6 hours prior to study.

Carbon-14 Breath Test - Radiopharmaceutical

- 1 uCi of C¹⁴ (5,730y t_{1/2}, 160 KeV) urea in capsule form administered P.O.
- C¹⁴ is a beta emitter = Liquid Scintillation Counter Required.
- Kit ordered from a Radiopharmacy includes a dose, standard, and balloons to trap exhaled carbon dioxide.

Carbon-14 Breath Test - Procedure

- Patient ingests C¹⁴-urea capsule with 20 mL of water, followed by another 20 mL of water in 3 minutes.
- Wait 10 minutes. Patient takes a deep breath, holds breath for 10 seconds and exhales into the first balloon provided.
- Wait 15 minutes. Patient takes a deep breath, holds breath for 10 seconds and exhale into second a balloon.

Carbon-14 Breath Test - Analysis

- Off- Site:
 - ◆ Balloons are sent back to the radiopharmacy for counting and reporting.
- On-Site:
 - ◆ Gas from balloon is transferred into a vial containing trapping fluid. Fluid changes color from blue => colorless.
 - ◆ Standard is prepared. Follow instructions provided in the kit.
 - ◆ Scintillation fluid is added into the sample vials and the standard vial.
 - ◆ All samples including background are counted for 10-20 minutes each in a scintillation counter.

Carbon-14 Breath Test – Calculation and Interpretation

- Standard is used to determine counter efficiency so that the CPM's could then be converted to DPM's.

Interpretation:

- ◆ < 50 dpm at 10 and 15 min collection:
negative for *H. pylori*.
- ◆ 50-199 dpm at 10 and 15 min collection:
indeterminate.
- ◆ >200 dpm at 10 and 15 min collection:
positive for *H. pylori*.

Carbon-14 Breath Test – Common Pitfalls.

- Causes of false negatives:
 - ◆ Antibiotics taken recently.
 - ◆ Bismuth, and proton pump inhibitors taken less than 2 weeks prior to study.
 - ◆ Inability to swallow capsules.
 - ◆ Non-fasting.
- Causes of false Positives:
 - ◆ Very rare, due to other bacteria that may metabolize the labeled urea.

Vitamin B12 Absorption (Schilling Test)

- Vitamin B12 is found in meat, milk and eggs.
- B12 is stored by the liver in very large quantities, released as per needed basis.
- In cases of B12 malabsorption, deficiency of the vitamin is not manifested for a long time due to high levels of stored amount.
- After ingestion, B12 is linked to intrinsic factor, which is produced by parietal cells in the stomach.
- B12 and intrinsic factor then pass into small intestine where B12 is absorbed into circulation.
- Without intrinsic factor, B12 is not absorbed and pernicious anemia will begin.
- Often, patients with pernicious anemia may have anti-parietal cells and anti-intrinsic factor antibodies, leading to intrinsic factor deficiency.

Vitamin B12 Absorption – Patient Preparation and Radiopharmaceuticals

- Patient NPO post midnight.
- No recent Nuclear Medicine Exams.

- 0.5uCi Co⁵⁷ labeled B12 (capsule form).
- Co⁵⁷: 270d half life, 122 keV.
- 1000 ug B12 flushing dose.

Vitamin B12 Absorption- Stage I

- Patient is interviewed, and procedure is explained. Labeled urine collection bottles are given to the patient for urine collection.
- Patient is administered 0.5 μCi $\text{Co}^{57}\text{B12}$ capsule; patient remains NPO for 2 hours.
- 1000 μg of regular B12 *flushing* dose is administered IM (intramuscular injection).
- Flushing dose of B12 will saturate all B12 binding sites and force the radioactive B12 to be excreted through urine.
- If $\text{Co}^{57}\text{B12}$ is not absorbed by the small intestine, it will never enter circulation and will be defecated out.
- After 48 hours patient will return the 24 hour and 48 hour urine collections to the nuclear medicine department.

Vitamin B12 Absorption – Stage I

Calculations:

- Total volume of each collection is recorded, and two 4 mL samples of each collection are drawn up into vials.
- Standard of 4 mL (supplied with the kit) prepared in a vial. Standard represents 1% of total administered dose.
- 4 mL of water is drawn up into a vial; will be used for background counting.
- All vials (samples, standard ad background) counted for 20 minutes each in order to obtain most accurate reading.

Vitamin B12 Absorption – Stage I: Interpretation of Results

$$\% \text{ excreted} = \frac{[\text{net cpm urine sample} / \text{net cpm std.}] / [(\text{urine sample} / \text{total sample volume}) / \text{std. dilution factor}]}{100}$$

- Negative : > 9% excretion. Test is finished
- Indeterminate: 6% - 9% excretion. Repeat test
- Positive: < 6% excretion. Proceed to Stage II

False positive:

- Missing urine collection.
- Renal failure.

False negative:

- Recent nuclear exam.
- Fecal contamination.

Vitamin B12 Absorption – Stage II:

- Performed if Stage I is positive.
- Patient may have anti-intrinsic factor antibodies, causing malabsorption of vitamin B12.
- Evaluate possible intrinsic factor deficiency.
- In Stage II, Co⁵⁷B12 capsule will be given together with intrinsic factor.
- Everything else remains the same as in Stage I.

Vitamin B12 Absorption – Stage II: Interpretation of Results

- Negative : > 9% excretion.
Test is finished, B12 is not absorbed due to intrinsic factor deficiency.
- Indeterminate: 6% - 9% excretion.
Repeat test.
- Positive: < 6% excretion.
Bacterial overgrowth possible. Patient will undergo a broad spectrum antibiotic treatment, and return for Shilling Test III.

Vitamin B12 Absorption – Stage III

- Stage III is performed after the patient undergoes antibiotic therapy if the bacterial overgrowth is suspected.
- Shilling Test I is then repeated.
- Normal excretion following antibiotics means that B12 malabsorption was due to bacterial overgrowth.

Vitamin B12 Absorption – Dual Isotope (Dicopac Method)

Overview:

- Combination of Stage I and Stage II.
- Same patient prep as in regular Stage I.
- $\text{Co}^{57}\text{B12}$ capsule bound with intrinsic factor. ($T^{1/2} = 270\text{d}$, 122keV).
- $\text{Co}^{58}\text{B12}$ capsule without intrinsic factor. ($T^{1/2} = 71\text{d}$, 810keV).
- Flushing dose of 1000 ug administered I.M.
- Urine collected 0-24 hours, and 24-48 hours.
- Total volumes are recorded, samples and std. are drawn up.
- Differential isotope counting is performed.

Interpretation of Results:

- $\text{Co}^{57} > 9\%$ AND $\text{Co}^{58} > 9\%$: NORMAL.
- $\text{Co}^{57} > 9\%$ AND $\text{Co}^{58} < 6\%$: LACK OF INTRINSIC FACTOR.
- $\text{Co}^{57} < 6\%$ AND $\text{Co}^{58} < 6\%$: BACTERIAL OVERGROWTH.

Total Blood Volume Determination

Conventional hematocrit may be inaccurate in cases of:

- Dehydration.
 - Increased plasma volume.
 - Polycythemia vera.
 - Splenomegaly.
-
- TPV : total plasma volume
 - TRCV : total red cell volume

Plasma Volume Determination

Isotope:

- I125 HSA (Human serum albumin). 10 uCi in 1.5 mL. A fraction of HSA does not remain within the intravascular space but diffuses into extravascular compartments.
- During analysis, the extrapolation technique is used to calculate the original plasma volume at time “zero”.

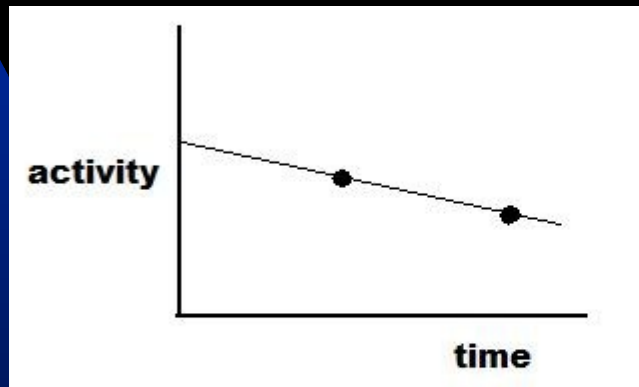
Patient Prep and Procedure:

- Patient did not have any recent NM Exams.
- Patient remains supine 15-30 min to ensure proper plasma mixing.
- Patients height, weight, and total volume and time of injection is recorded.
- 3 samples of 10 mL of whole blood collected at 10, 20, 30 minutes (heparinized syringe).
- Standard of 10uCi of I125 HSA is prepared.
- Use opposite arms for injection and samples drawing.
- Use large bore needles.

Plasma Volume Determination

Calculation:

$TPV = (\text{volume injected} \times \text{net standard activity}) / \text{net patient activity at time zero.}$



Sources of Error:

- Infiltration of the dose: overestimated results.
- Previous Nuc. Med. Exam: underestimated results.

Note: Test is often coupled with Red Cell Volume Determination.

Red Cell Volume Determination

- All red cells of random age are labeled with this procedure. Aka: random labeling.

Isotope:

- 10 – 20 uCi of Cr^{51} 27.7 day $t_{1/2}$, 320 KeV.

Patient Prep:

- Same as Plasma volume determination.

Red Cell Volume Determination – Labeling Techniques

Ascorbic Acid Labeling Method

1. 10 mL of whole blood drawn. Use 2.0 mL of ACD not Heparin.
2. Add 30 μCi of Cr^{51} .
3. Incubate for 30 min at room temperature.
4. 50 mL of Ascorbic Acid is added to reduce Chromate ions to Chromic ions, which will stop further labeling to RBC's.
5. 80% - 95% of tag is achieved.
6. Re-inject 10-20 μCi , keep the rest for standard.

Red Cell Volume Determination

Patient Prep and Procedure.

- No previous Nuc Med exams.
- Patient supine 15-20 min prior to exam.
- Inject 10-20uCi of Cr⁵¹ RBC's.
- Use different arms for injections and sample drawing.
- Draw samples into heparinized syringes at 10 and 20 min.
- Prepare standard using remaining Cr⁵¹ RBC's.
- Count all samples including background.
- Follow included worksheet in the kit for analysis.

Sources of Error.

- Infiltration of the dose: overestimated results.
- Previous Nuc. Med. Exam: underestimated results.

Total Blood Volume Analysis

Normal Values (mL/kg).

	Men	Women.
Total Blood Volume	55-80	50-75.
Total Red Cell Volume	22-35	20-30.
Total Plasma Volume	30-45	30-45.

Results are dependent on sex, disease state, metabolic rate, and overall body habitus.

Red Cell Survival

- Determines the mean survival time of Cr⁵¹ RBC's in patients with hemolytic anemia.

Radioisotope:

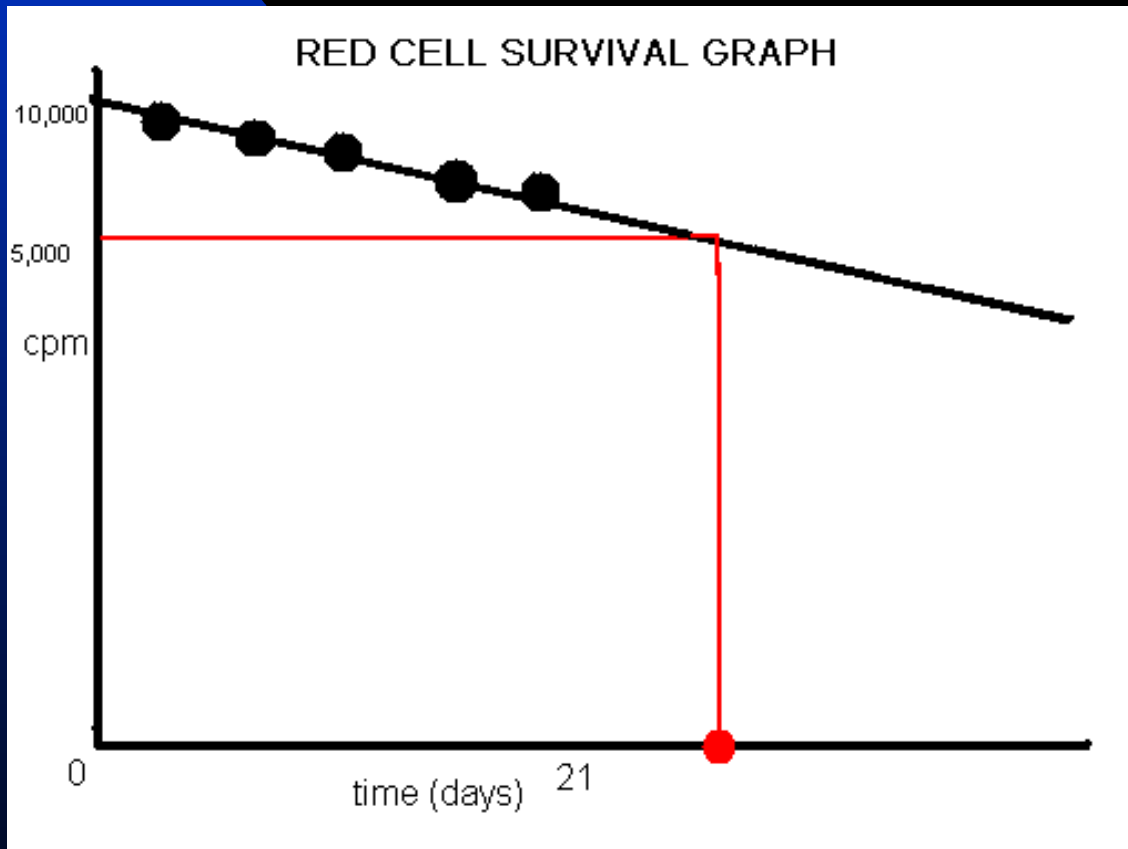
- Cr⁵¹ RBC (ascorbic acid labeling technique).
- 1.5 uCi Cr⁵¹ RBC per kg, minimum of 50 uCi.

Red Cell Survival

Patient Prep and Procedure.

- Follow Cr⁵¹ RBC tagging technique using ascorbic acid.
- Inject the dose, patient returns 24 hours later.
- 24 hour period allows for any damaged Cr⁵¹ RBC's to be eliminated from circulation.
- Draw 5 mL sample at 24 hours and every other day for the next 3 weeks.
- Count all samples, and plot results on graph.

Red Cell Survival



Graph Interpretation

1. Plot sample results, interpolate value for time 0.
2. Divide time 0 value by 2.
3. Draw horizontal line from the value in step 2 until it intersects with the graph.
4. Drop a vertical line to determine time value for mean survival rate of RBC's.

Red Cell Survival

Normal Values.

True mean survival rate of RBC's = 50 – 60 days.

However:

1% of RBC's is removed from daily circulation,

1% of Cr⁵¹ is released from tagged RBC's daily.

Factoring in lost activity, will produce Nuclear Medicine survival rate to 25 – 35 days.

Therefore: 25 – 35 days = 50 – 60 days.

N. M. = Physiological.

Sources of Error.

- Loosing blood during 3 weeks decrease survival time.
- Receiving blood transfusions will increase survival time.

Splenic Sequestration

- Performed if Red Cell Survival test is abnormal to rule out spleen as a possible source of problem. May be performed together with Red Cell Survival test.

Isotope:

- Cr⁵¹ RBC's labeled with ascorbic method.

Procedure:

- Scintillation probe with collimator required to filter out scatter.
- Patient returns to department in 24 hours and every other day after injection of the isotope.
- Areas of spleen, precordium and liver are marked with permanent marker, to be counted every visit. Positioning and geometry of scintillation probe must be the same every time.

Splenic Sequestration

Interpretation of Results

Normal:

- Liver to precordium ratio is 0.5
- Spleen to precordium ratio 0.5 – 1.0

Abnormal:

- Initial Spleen to precordium ratio 2.0 and gradually rising over time indicates increased splenic blood pool.

Sources of error:

- Inconsistent positioning, inconsistent results.
- Blood transfusions, blood loss will affect results.

Thyroid Uptake

- Used to measure thyroid function.
- Thyroid produces T3 and T4 hormones which control many metabolic functions.
- Thyroid uptake is usually performed together with a scan to further aid in diagnosis.

Thyroid Uptake

Indications

- Hyperthyroidism
- Hypothyroidism
- Thyroiditis
- Goiters
- Post treatment follow-up

Isotope

- | | | |
|---------|-------------|---------------------|
| ■ I 123 | 100-200 uCi | 159 KeV, 13 hr T1/2 |
| ■ I 131 | 10-15 uCi | 364 KeV, 8 d T1/2 |

Thyroid Uptake

Patient Prep

- Iodine free diet for 3 weeks
- No I.V. contrast for 4 weeks
- Off thyroid controlling medications.
- Off multi-vitamins for 4 weeks
- Patient NPO post midnight

Thyroid Uptake

Procedure

- Patient is administered a Radioactive Iodine capsule and is instructed to return 6 and 24 hours later for thyroid counting.

1 Pill Method:

- Iodine capsule is counted and administered to the patient. Decay correction is applied to the exact time the patient returns for counting.

2 Pill Method:

- 2 identical pills are ordered. One is administered to the patient, the second remain in the department as the standard. When the patient returns the standard is then counted.

Thyroid Uptake

Normal Values:

- Depend on the population serviced by the facility.
- Usually 15% - 35% is considered normal.
- < 15% is hypothyroidism.
- > 35% is hyperthyroidism.

Sources of Error:

- Free Iodine in the system will compete with the Radioactive capsule.
- Ectopic tissue should be ruled out.
- Geometry must be observed correctly.

References

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