

AZIMAT NUCLEAR MEDICINE

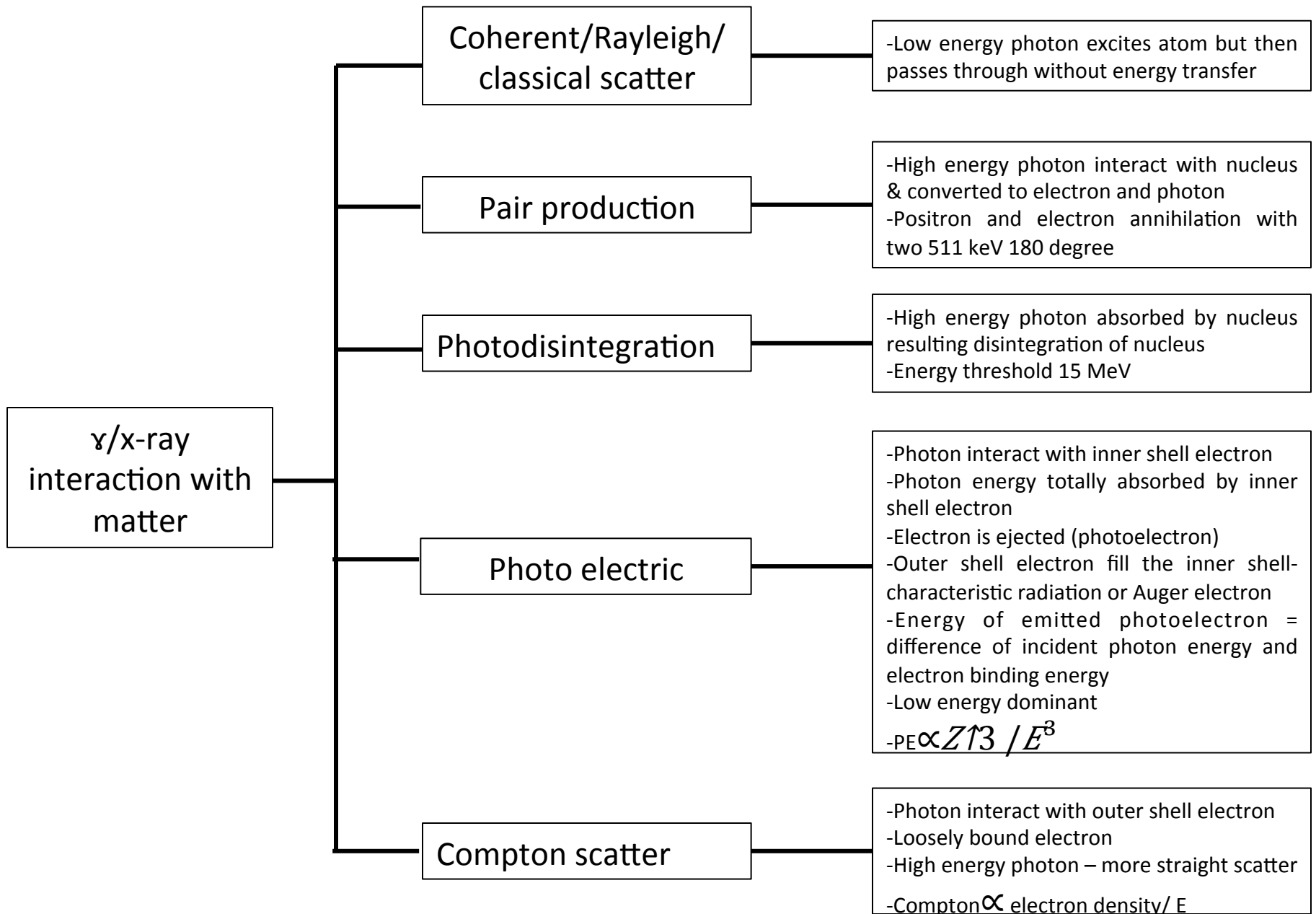
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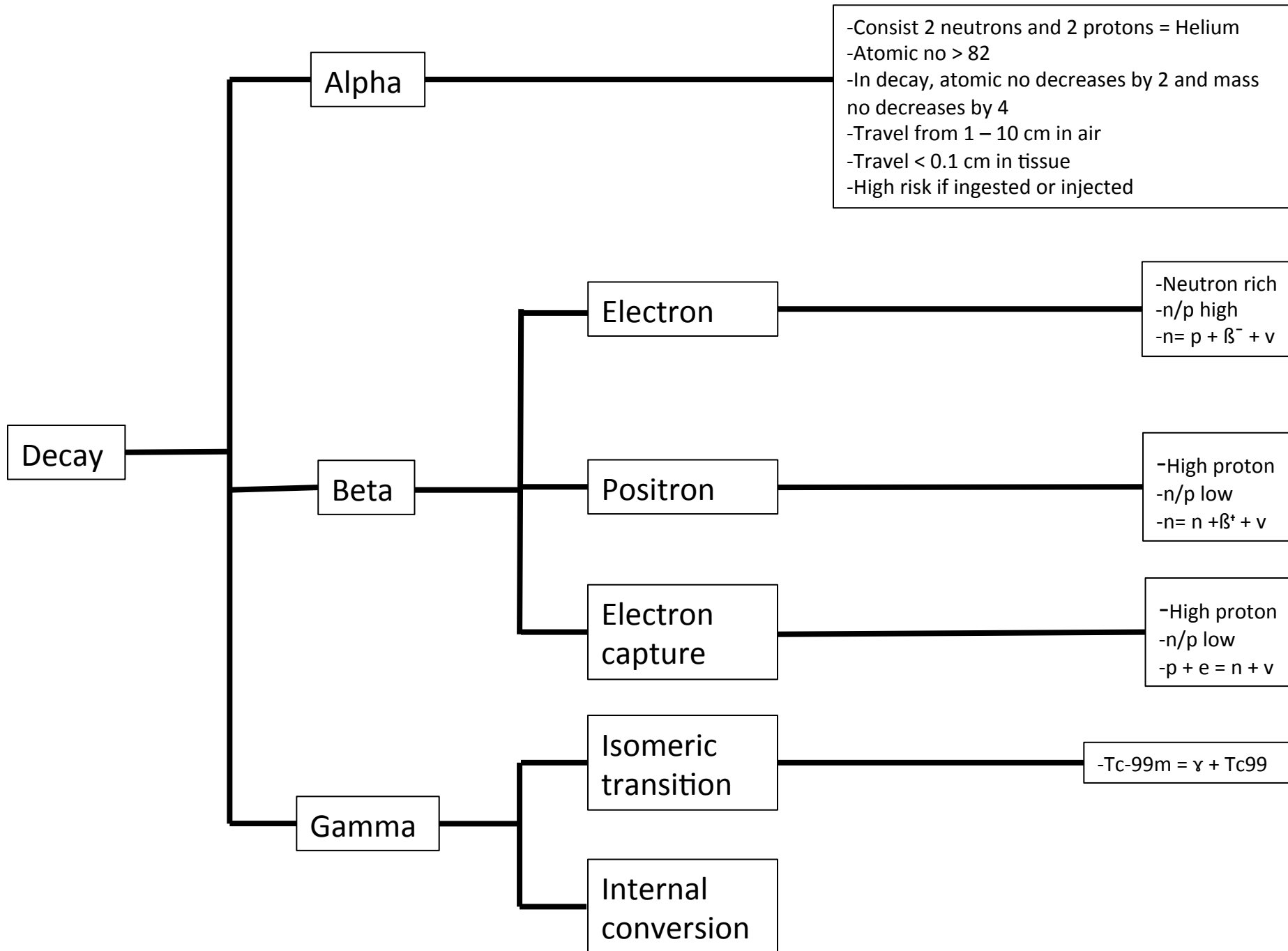
DR ZOOL HILMI

2013

SIMPLE PHYSIC

Radionuclide	Decay mode	Half time	Energy (keV)	Production method
Thallium-201	Electron capture	73.1 hr	69-83(94%) , 135(3%) 167(10%)	Cyclotron
Gallium-67	Electron capture	78.3 hr	93(37%),185(20%), 300(17%),395(5%)	Cyclotron
Indium-111	Electron capture	2.8 d	171(90%),245(94%)	Cyclotron
Iodine-123	Electron capture	13.2 hr	159	Cyclotron
Iodine-131	Beta minus	8 d	364	Reactor
Technetium-99m	Isomeric transition	6 hr	140	Generator
Cobalt-57	Electron capture	272 d	122	Cyclotron
Fluorine-18	Positron emitting	110 min	0.653 MeV	Cyclotron
Gallium-68	Positron emitting	68 min	1.9 MeV	Generator
Carbon-11	Positron emitting	20 min	0.96 MeV	Cyclotron
Nitrogen-13	Positron emitting	10 min	1.19 MeV	Cyclotron
Oxygen-15	Positron emitting	2 min	1.70 MeV	Cyclotron
Rubidium-82	Positron emitting	1.3 min	3.15 MeV	Generator





Q = EXPOSURE

AMOUNT OF ELECTRICAL CHARGE PRODUCED BY IONIZING ELECTROMEGNETIC RADIATION PER MASS OF AIR

UNIT = C/Kg = Roentgen
1 R = 2.58×10^{-4} C/Kg

D = ABSORB DOSE

DIRECTLY IONIZATION CHARGE PARTICLE DEPOSIT ENERGY BY (EXCITATION/IONIZING) PER UNIT MASS

UNIT = J/Kg
1 Gray = 1 J/ Kg
100 rad = 1 Gray
Rad = RADIATION ABSORB DOSE

H = EQUIVALENT DOSE

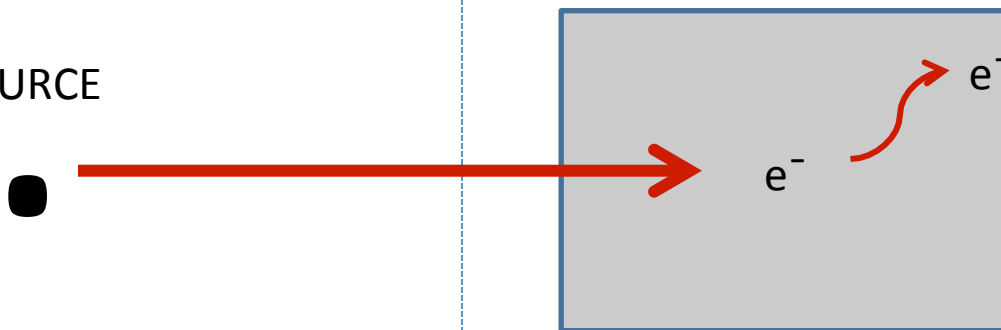
ICRP 1990
MEASURE OF RADIATION SPECIFIC BIOLOGIC DAMAGE IN HUMAN

UNIT = Sievert
100 rem = 1 Sv = J/Kg

WR = RADIATION WEIGHTING FACTOR

XRAY/ γ / β /e	= 1
PROTON > 2 MeV	= 5
NEUTRON	= 5 – 20
ALPHA	= 20

SOURCE



SKIN DOSE

RADIATION EXPOSURE INCIDENT TO PATIENT DUE TO RADIOLOGICAL EXAMINATION

CHEST X RAY = 0.1 – 0.2 mGy
SKULL = 1.5 mGy
ABDOMEN = 3 mGy
LUMBAR = 10 mGy

K = KERMA

ENERGY CARRIED BY PHOTON (OR OTHER INDIRECT IONIZING RADIATION) TRANSFER ENERGY TO CHARGE PARTICLE (PE/COMPTON/ PAIR PRODUCTION

UNIT = J/Kg OR Gray

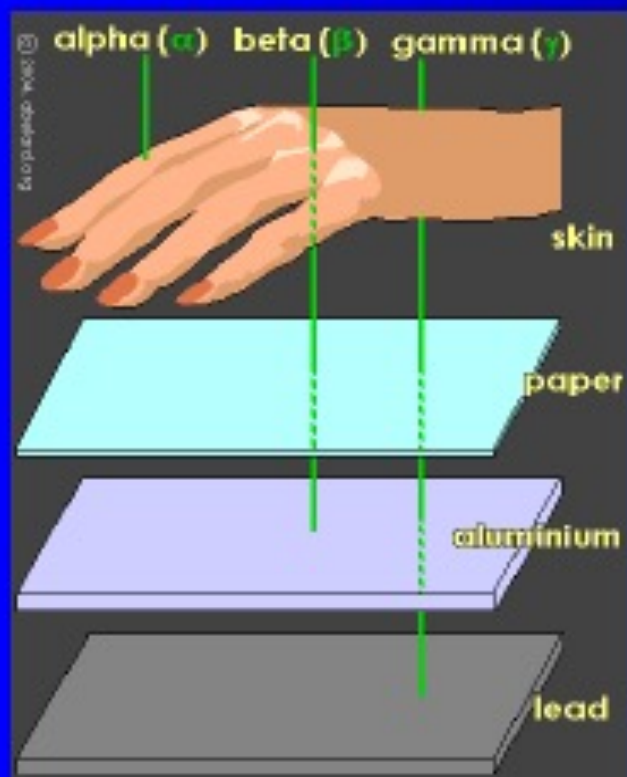
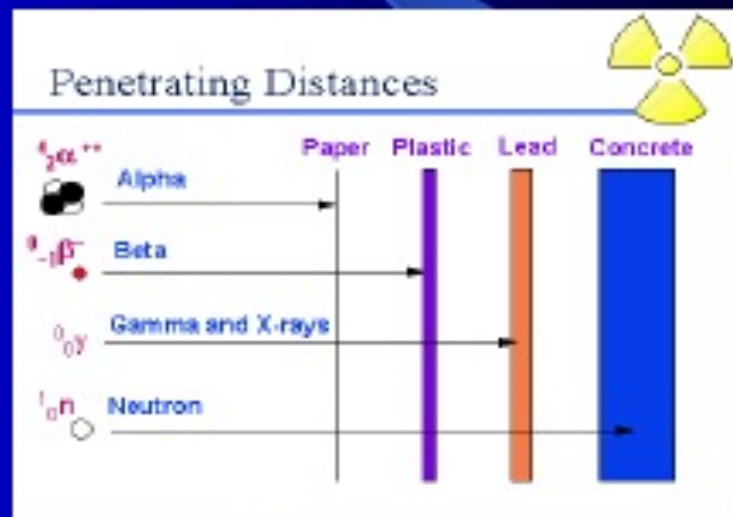
E = EFFECTIVE DOSE

ICRP 1990
MEASURE OF RADIATION AND ORGAN SYSTEM SPECIFIC DAMAGE IN HUMAN

UNIT = Sievert
100 rem = 1 Sv = J/Kg

WT = TISSUE WEIGHTING FACTOR
GONAD = 0.2
BONE MARROW/LUNG/STOMACH/ COLON = 0.12
BLADDER/BREAST/LIVER/THYROID = 0.05
SKIN/BONE = 0.01

WHAT STOPS THEM !!!



PARATHYROID SCINTIGRAPHY

Pearls & Pitfalls

Parathyroid imaging

- The most common indication for parathyroid imaging is to localize the hyperfunctioning gland (adenoma) either in the thyroid bed or in the ectopic location (lower neck or mediastinum)
- Parathyroid adenomas are usually single
- Parathyroid imaging is usually performed by using Tc-99m sestamibi with sequential images after 2 hours, whereas parathyroid adenomas usually hyperconcentrate Tc-99m sestamibi and persist over time

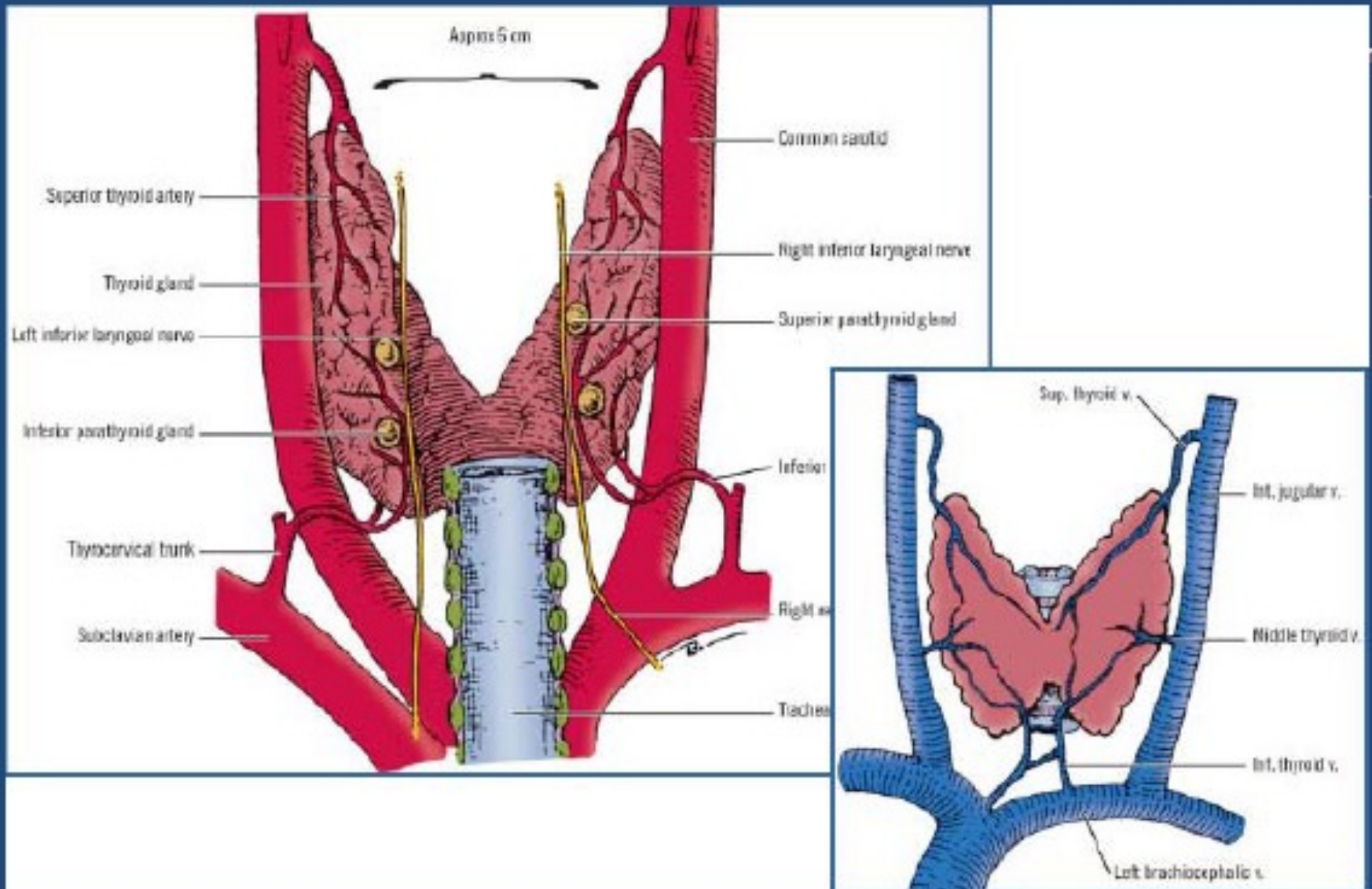
PARATHYROID SCINTIGRAPHY

ANATOMY AND EMBRYOLOGY

ANATOMY

- 4 parathyroid glands
- Measuring 6mm x 3mm
- Weighing 35 – 40 gram
- Rarely, may be only 2 glands or as many as 8 glands

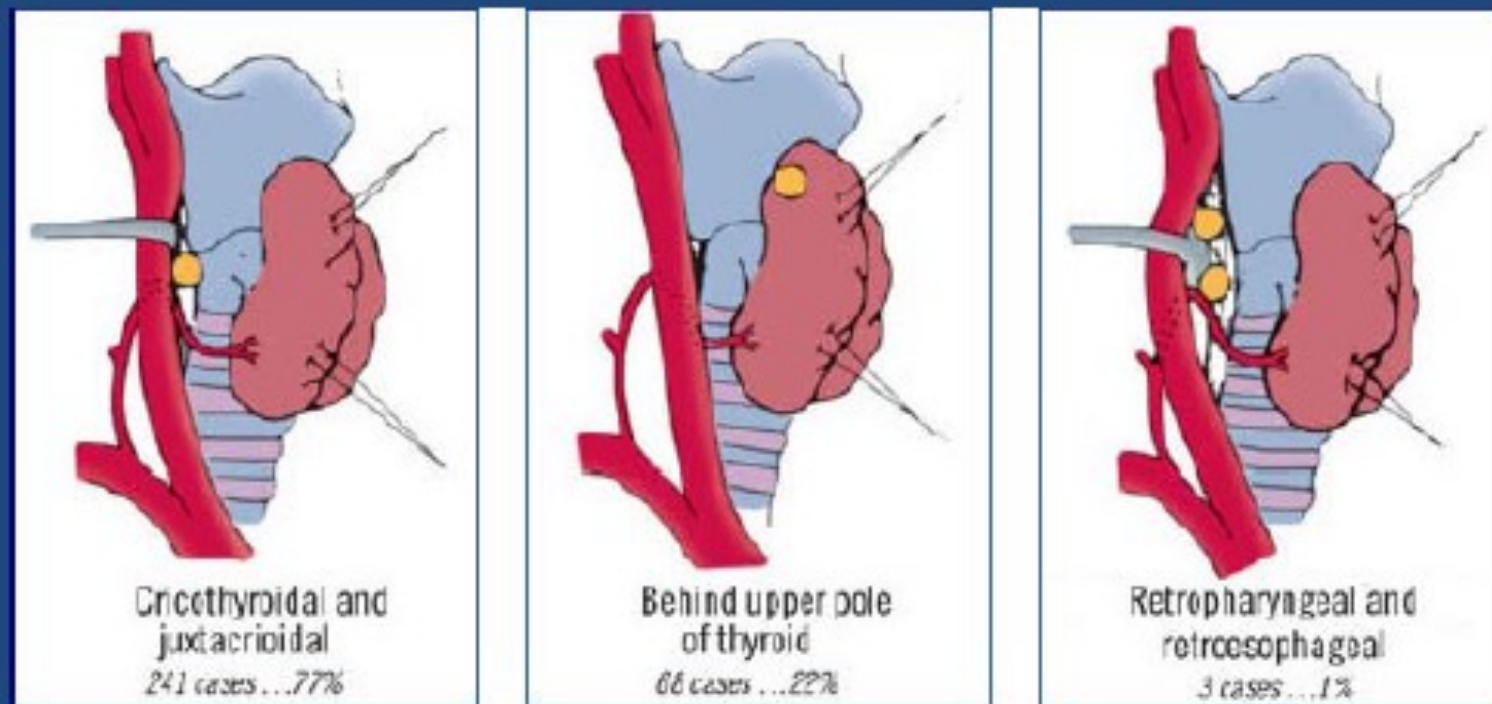
Anatomy



EMBRYOLOGY

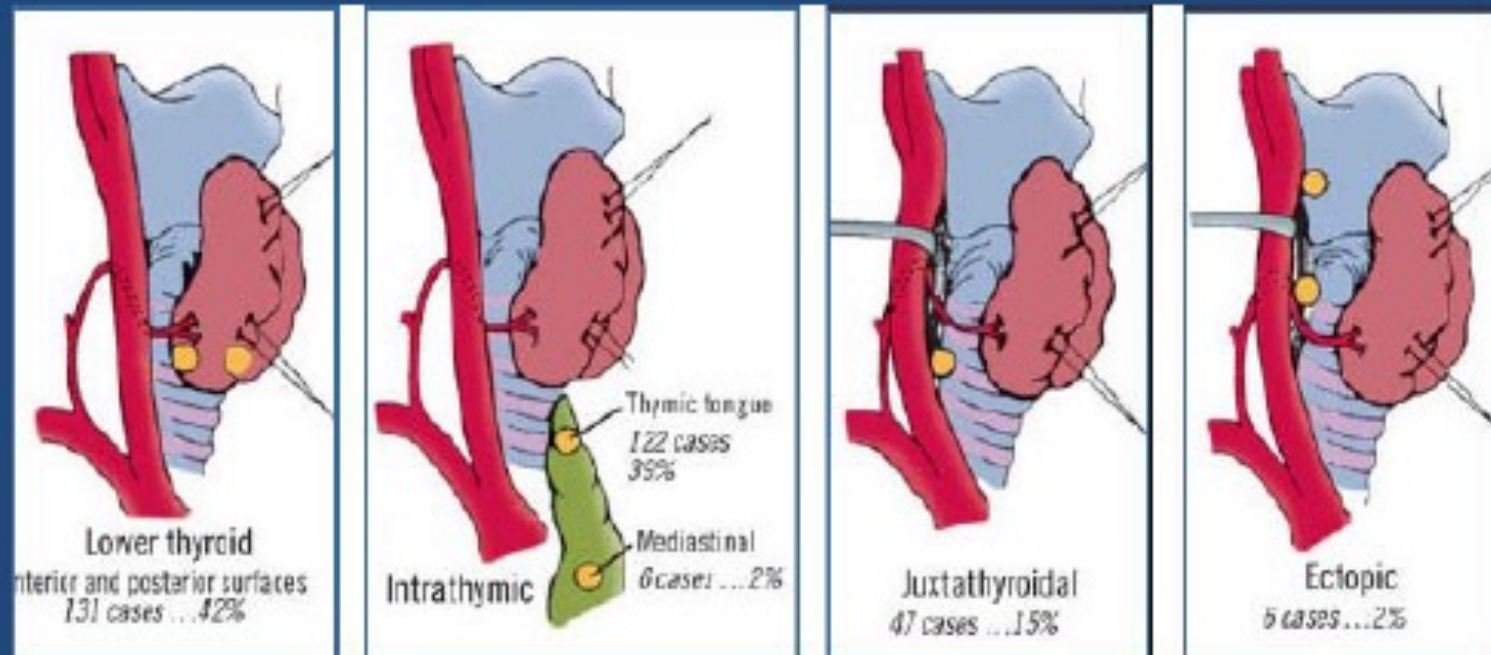
- *Inferior parathyroid glands* arise from 3rd branchial pouch and migrate caudally with the thymus
- *Superior glands* arise from 4th branchial pouch and migrate with the thyroid

Superior parathyroid location



Sedgwick and Cady. Surgery of the thyroid and parathyroid glands

Inferior parathyroid location

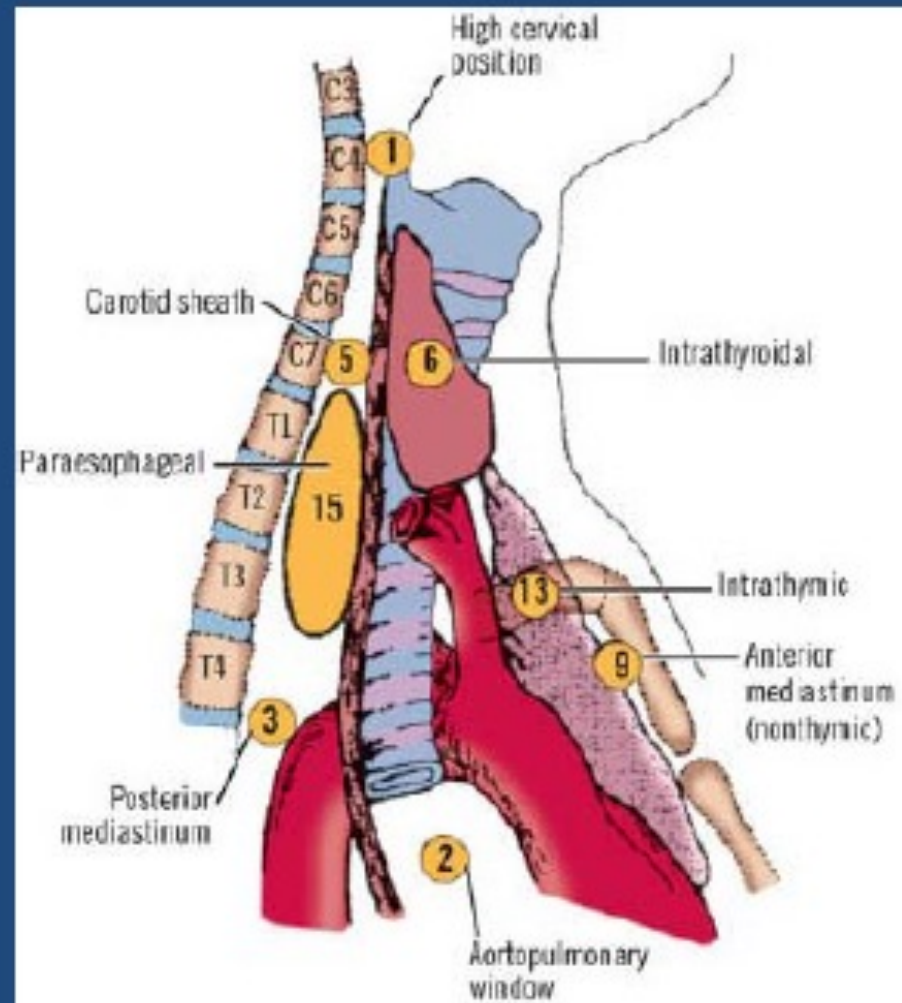


Sedgwick and Cady. Surgery of the thyroid and parathyroid glands.

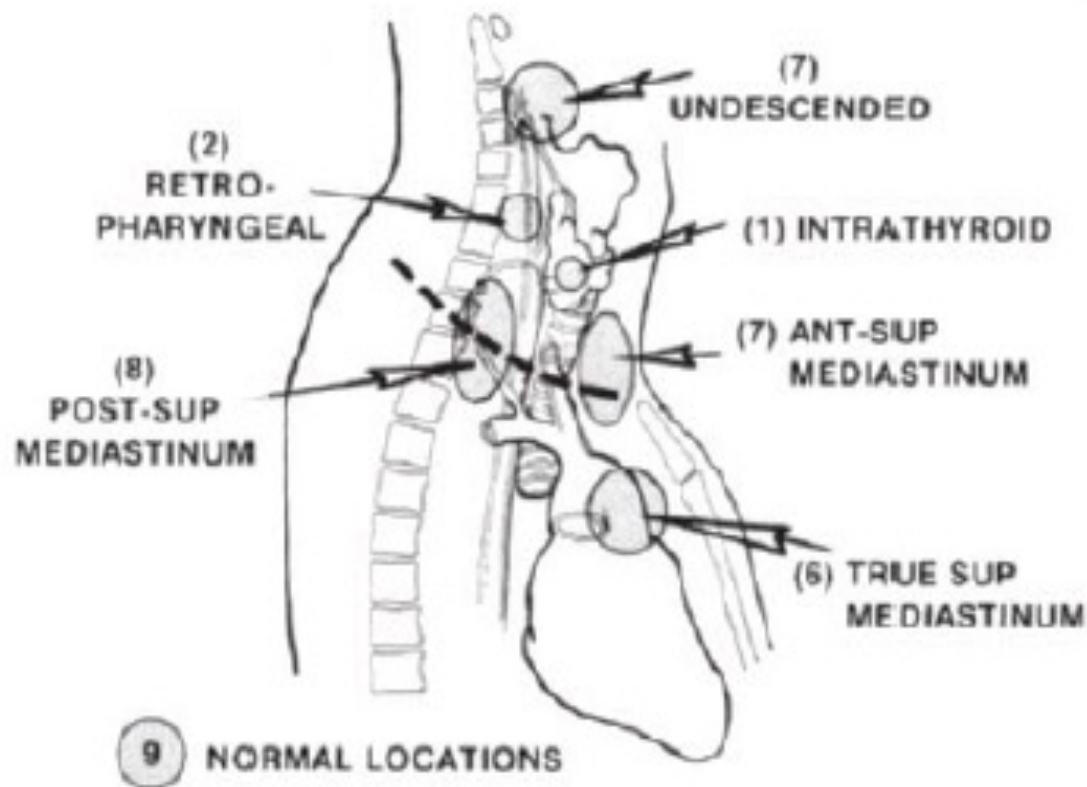
Anatomy

Ectopic tissue

- Anterior mediastinum
- Posterior mediastinum
- Aorto-pulmonary window
- Pericardium
- Carotid sheath
- Pharyngeal submucosa



Ectopic ?



Distribution of the ectopic sites of parathyroid adenomas

Type of cells in parathyroid

1. **Chief cell** – produces parathyroid hormone (PTH) and it has little mitochondria or cytoplasm
2. **Oxyphil cell** – high number of mitochondria.

Pathophysiology

- Hyperpathyroidism :
 1. **Primary** hyperpathyroidism
 2. **Secondary** hyperpathyroidism
 3. **Tertiary** hyperpathyroidism

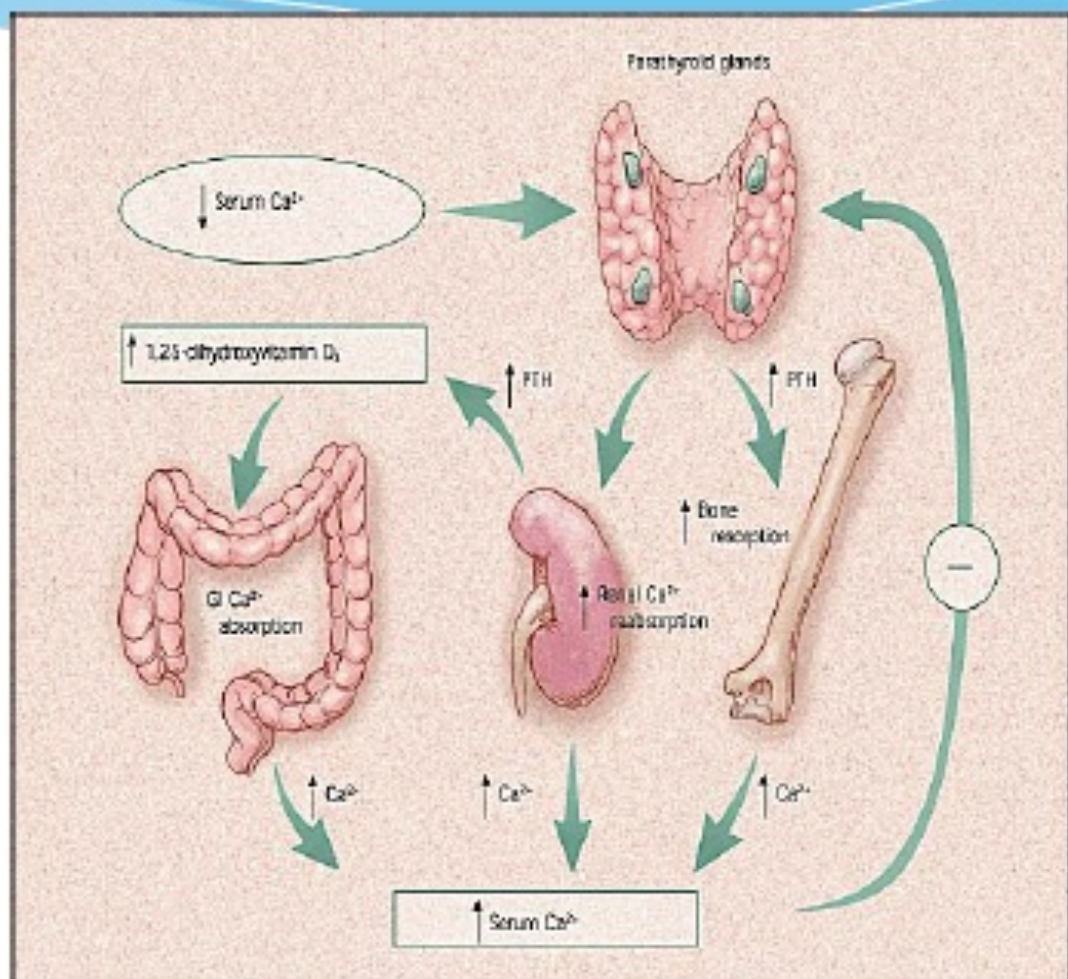
PTH/Calcium Homeostasis

Low circulating serum calcium concentrations stimulate the parathyroid glands to secrete PTH, which mobilizes calcium from bones by osteoclastic stimulation.

PTH also stimulates the kidneys to reabsorb calcium

PTH convert 25-OH Vit D₃ (produced in the liver) to the active form, 1,25-diOH D₃, which stimulates GI calcium absorption.

High serum calcium concentrations have a negative feedback effect on PTH secretion.



Hyperparathyroidism

- Chief cells (single or multiple glands) synthesis more and release more PTH
- PTH synthesize, stored and secreted by parathyroid glands
- PTH responsible for calcium and phosphorus homeostasis by its action on bone, small intestine and kidneys

Primary Hyperparathyroidism

- Estimated incidence is 1 case per 500 general population
- Incidence increases above age 40
- Most patients with sporadic primary hyperparathyroidism are postmenopausal women with an average age of 55 years

Causes of excess PTH production

Primary Hyperparathyroidism

- 90% : 1 overactive gland
(single adenoma)
- 8.5% : 2 or 3 glands
(multiple adenomas)
- 2.5% : 4 overactive glands
(four-gland hyperplasia)
- <1% : cancer

Causes of excess PTH production

Secondary Hyperparathyroidism

- Due to exogenous defects
 - Chronic renal dysfunction
 - Calcium and vitamin D deficiency
 - Reduced intestinal calcium absorption
 - Bone resistance to PTH
 - Renal phosphate retention

Causes of excess PTH production

Tertiary hyperparathyroidism

- Persistent 2° hyperparathyroidism leading to autonomous oversecretion of PTH after correction of the primary cause

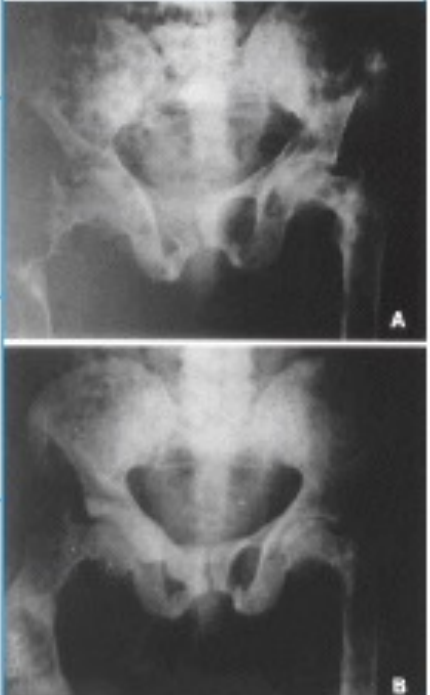
Hyperparathyroidism: Clinical features

Majority of patients are asymptomatic

Renal	GIT	CNS	others
Polyuria	Anorexia	Confusion	Pruritus
Polydipsia	Vomiting	Lethargy	Sore eyes
	Constipation	Depression	Bone ache
	Abdominal pain		

Hyperparathyroidism: Clinical features

End Organ Damage

Bone	Kidneys	Joints	Pancreatitis
Osteoporosis	Renal calculi	Chondro-calcinosis	
Xray changes	Nephro-calcinosis	Pseudogout	
Osteitis fibrosa cystica	Renal impairment		

Clinical Indications for Parathyroid Localization

- To localize hyperfunctioning parathyroid tissue (adenomas or hyperplasia) in primary hyperparathyroidism
- To localize hyperfunctioning parathyroid gland or ectopic parathyroid tissues prior to surgery
- To localize hyperfunctioning parathyroid tissue (usually adenomas) in patients with persistent or recurrent disease

Localization of the Parathyroids

Nuclear Medicine techniques

- ^{75}Se selenomethionine
- $^{201}\text{Tl}/^{99\text{m}}\text{Tc}$ pertechnetate subtraction scanning
- $^{99\text{m}}\text{Tc}$ -sestamibi scanning
- $^{99\text{m}}\text{Tc}$ tetrofosmin subtraction technique
- PET : probably best reserved for those patients who had failed surgical procedure and localization with $^{99\text{m}}\text{Tc}$ sestamibi

PARATHYROID IMAGING-1

Table 1. Protocol of Imaging

Single tracer dual-phase	Dual tracer subtraction
Tc-99m MIBI early/delay	Tl-201/Tc-99m (I-123)
Tc-99m Tetrofosmin early/delay	Tc-99m MIBI/Tc-99m (I-123)

Tc MIBI scintigraphy is superior to 201-thallium and 99m-technetium pertechnetate (Tl - Tc) subtraction imaging and the gold standard for pre-operative localization of hyperfunctioning parathyroid tissue



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Radiopharmaceuticals

^{201}Tl -Chloride

Physical half-life	72 h
Energy	69–83 keV (94% abundance); 167 keV (10% abundance) 135 keV (3%)
Dose	2–3.5 mCi intravenously
Uptake	Nonspecific tumor imaging agent <ul style="list-style-type: none">- Blood flow- Depends on the Na-K-ATPase pump on the cell membrane- Remains free in the cytosol

^{201}Tl Chloride taken up by both abnormal parathyroid tissue and thyroid tissue in proportion to blood flow

Radiopharmaceuticals

^{123}I Sodium Iodide

Physical half-life	13.2 h
Energy	159 keV
Dose	200-550 uCi p.o. when using $^{99\text{m}}\text{Tc}$ sestamibi
Uptake	Thyroid imaging agent - Trapping and organification

Radiopharmaceuticals

^{99m}Tc -Pertechnetate

Physical half-life	6 h
Energy	140 keV
Dose	2–4 mCi when using ^{201}Tl chloride 5–10 mCi when using ^{99m}Tc sestamibi
Uptake	trapped by functioning thyroid tissue
^{99m}Tc sestamibi has a higher total activity in the thyroid gland than ^{201}Tl chloride	

Radiopharmaceuticals

^{99m}Tc -Sestamibi

Physical half-life	6 h
Energy	140 keV
Dose	20 mCi IV
Uptake	Positive charge and lipophilic properties lead to passive diffusion into cytoplasm and mitochondria Large number of mitochondria oxyphil cells of parathyroid adenomas responsible for the avid uptake and slow release
^{99m}Tc sestamibi localizes in both parathyroid tissue and functioning thyroid tissue	

Radiopharmaceuticals

^{99m}Tc Tetrofosmin

Physical half-life	6 h
Energy	140 keV
Dose	20 - 25mCi IV
Uptake	Similar to sestamibi

** The thyroid washout rates are slower for ^{99m}Tc tetrofosmin than for ^{99m}Tc sestamibi.

** Earlier imaging findings are more diagnostic than delayed imaging findings

Single tracer dual phase method -1 PRINCIPLES

Tc-99m MIBI (or Tc-99m Tetrofosmin) uptake in thyroid tissue cleared more quickly than that in parathyroid tissue.

Sestamibi is a monovalent lipophilic cation that diffuses passively through cell membranes and accumulates almost exclusively in mitochondria following negative membrane potentials.



Single tracer dual phase method -2

- High mitochondria activity → increased in sestamibi uptake in primary hyperparathyroidism.
- The uptake is influenced by a few factors include :
 - Size of adenoma
 - The cell type (oxyphil rather than chief cells).



P-glycoprotein expression

Single tracer dual phase method -3 TECHNIQUES

- Early image at 10-15 minutes
- Static anterior chest and neck
- Delay images at 2-3 hrs (look for washout)



^{99m}Tc Sestamibi or Tetrofosmin Dual-Phase Parathyroid Imaging: Protocol Summary

Patient preparation	none
Administered dose	20 mCi IV
Patient position	Supine with the chin up and neck extended ROI: neck and mediastinum
Time of imaging	Early scan at 10 - 15 minutes Delayed scan at 1.5 – 2.5 hours
Imaging procedure	Use high-resolution parallel hole collimator 20% window centered at 140 keV Obtain anterior and 45° left and right anterior oblique views 300k per view.
SPECT imaging	dual headed SPECT camera: 360-degree contoured acquisition arc, 3-degree angular Sampling increment, 15-30-sec per view 128x 128 matrix 1.5 zoom (hanning or butterworth filter) Reconstruct transaxial, coronal and sagittal planes Reproject images at each sampling angle

Single tracer dual phase method -4 INTERPRETATIONS

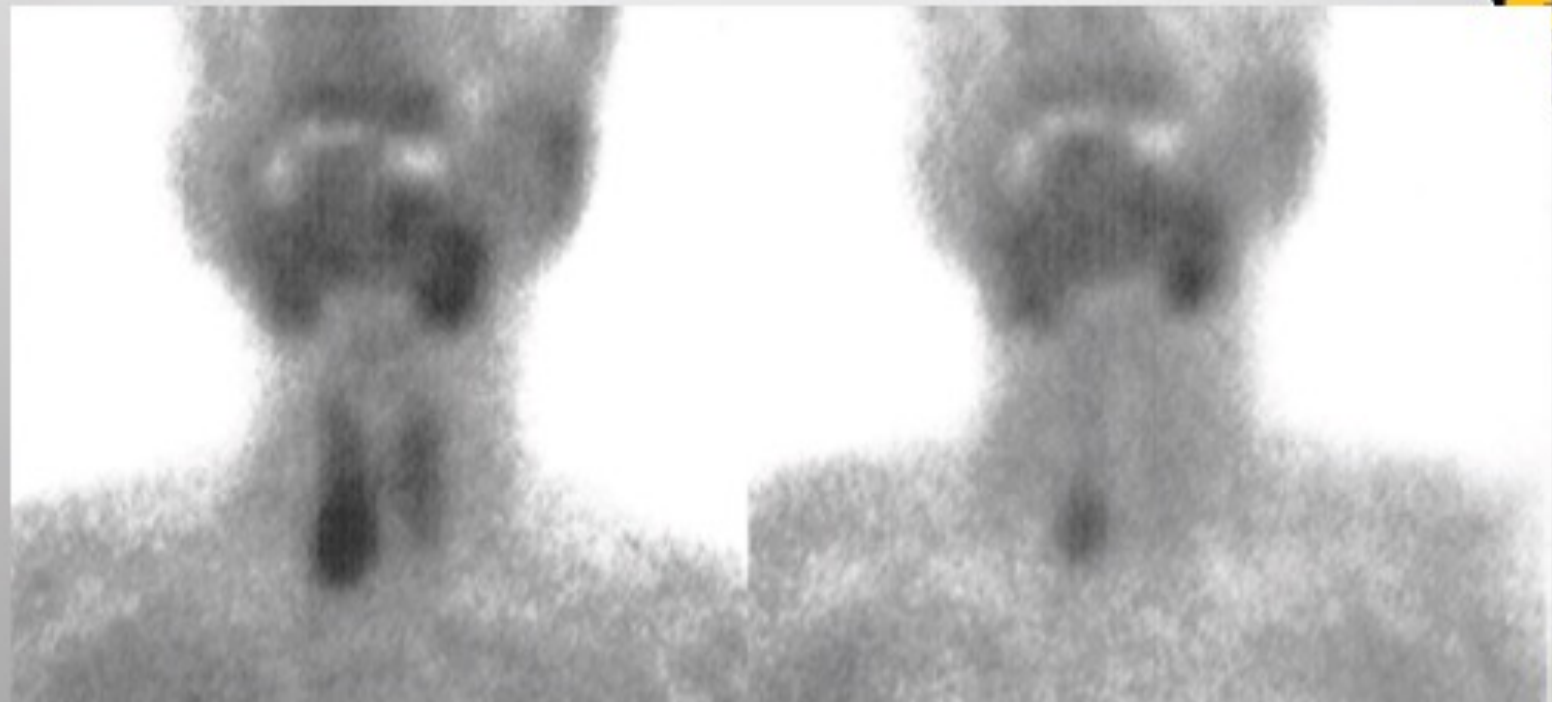
- A SOLITARY focus of increased tracer uptake with delayed washout in delay images characterizes a parathyroid adenoma.
- > 1 foci of such → hyperplasia or multiple adenoma





- **Normal parathyroid scan.**
- An immediate ^{99m}Tc -sestamibi image of the chest and neck shows activity in the parotids, salivary glands, thyroid and left ventricle.
- On the 2-h image the thyroid activity has faded almost completely, whereas the other areas remain mostly unchanged. The individual normal parathyroid glands are not seen.

Parathyroid adenoma



• 15 minutes

• 2 hours



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Single tracer dual phase method

LIMITATIONS



- False Negatives
 - Small adenomas*
 - Low mitochondrial contents
 - P-glycoprotein expression
- False positive
 - Hyperplastic thyroid nodules
 - Chronic autoimmune thyroiditis
 - Hurthle cell lesions
 - Browns tumors



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LIMITATIONS

- Delayed tracer washout from the thyroid parenchyma:
 - Thyroid diseases
 - MNG
 - Hashimoto thyroiditis
 - Thyroid adenoma
 - Thyroid carcinoma



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Dual tracer subtraction method-1 PRINCIPLES & TECHNIQUES



- The visualization of the thyroid gland with either Tc-99m pertechnetate or I-123 and then subtracting this image from an image of the Tl-210 or Tc-99m MIBI (or Tc-99m Tetrofosmin) uptake within the thyroid and parathyroid gland



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- 
- 
- 1st: ^{99m}Tc sestamibi or tetrofosmin
 - Visualization of thyroid and parathyroid
 - 2nd: $\text{I-}^{123}\text{I}$ or ^{99m}Tc pertechnetate
 - Visualization of thyroid only
 - Digitally subtracted (1-2)

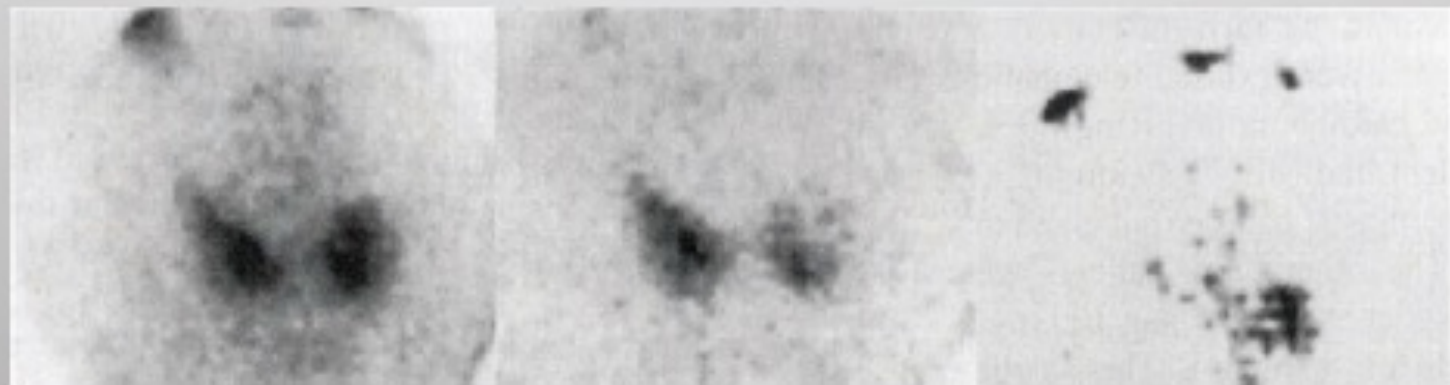
^{99m}Tc-pertechnetate/^{99m}Tc-Sestamibi Dual-Isotope Parathyroid Imaging: Protocol Summary

Patient preparation	none
Administered dose	^{99m} Tc-pertechnetate 5 – 10 mCi IV (or ¹²³ I 200-550uCi po) ^{99m} Tc-sestamibi 20 mCi IV
Patient position	supine with the chin up and neck extended ROI: neck and mediastinum
Time of imaging	^{99m} Tc pertechnetate : 30 min post-injection ^{99m} Tc sestamibi : 10-15 minutes
Imaging procedure	high-resolution parallel hole collimator ; pinhole also helpful ^{99m} Tc-pertechnetate:/sestamibi : 140 keV ± 20% window : high-count (10-min) image
SPECT imaging	dual headed SPECT camera: 360-degree contoured acquisition arc, 3-degree angular Sampling increment, 15-30-sec per view 128x 128 matrix 1.5 zoom (hanning or butterworth filter)

Image Acquisition

- Either pertechnetate or ^{123}I can be given first or pertechnetate given after sestamibi administration
- ^{123}I cannot be given after sestamibi because of the long time needed for localization
- If pertechnetate is injected after sestamibi, the patient should be immobilized for 15-30 min after pertechnetate has been injected, and then a 10-min image is acquired

Dual tracer subtraction method-2 INTERPRETATIONS



• 15 min Pertechetate Substraction



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Dual tracer subtraction method-3 LIMITATIONS



- I-123

- Not available on daily basis
- More expensive
- Longer half-life

- $^{99m}\text{TcO}_4$

- Thyroid activity was relatively high
- In some cases, it may mask relatively low ^{99m}Tc -sestamibi/tetrofosmin uptake from the parathyroid adenoma which is usually located behind the thyroid



Sources of Error

- Patient motion
- Image misregistration
- Adenomas or hyperplastic glands <500 mg in size
= difficult to detect
- Ectopic adenomas = difficult to detect
- Lesions of the thyroid, such as adenomas and carcinomas, may be indistinguishable from parathyroid adenomas
- Parathyroid carcinomas are also indistinguishable from parathyroid adenomas

Degree of Confidence

Dual-isotope technique (^{99m}Tc -sestamibi/ ^{99m}Tc -pertechnetate or ^{123}I)

- Sensitivity = 90 – 100 %

Dual-phase technique (^{99m}Tc -sestamibi)

- Sensitivity = 70 – 100 %

Early SPECT

- Sensitivity = 91 – 96 %

Comparison of Pertechnetate / Thallium Parathyroid Scintigraphy with Other Imaging Techniques

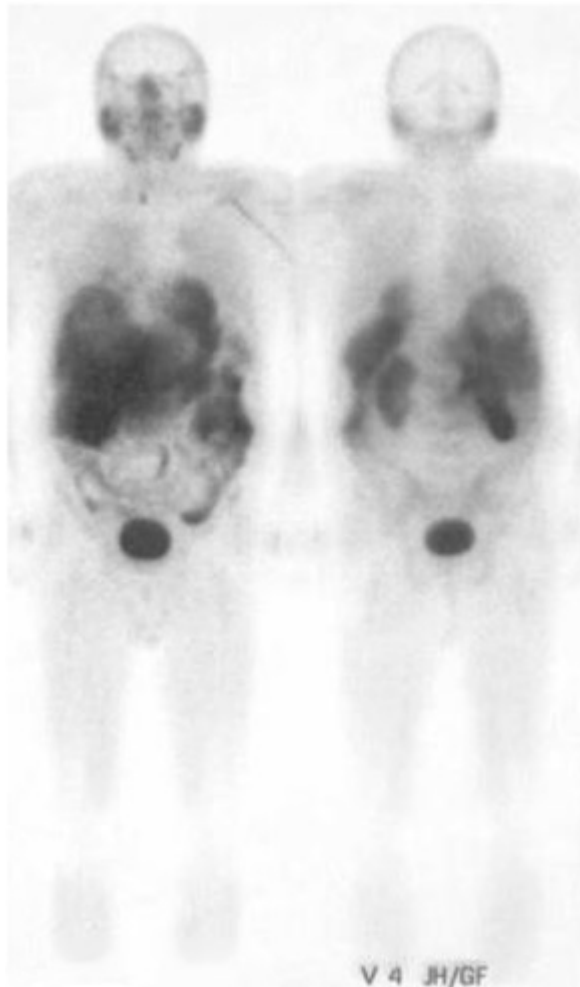
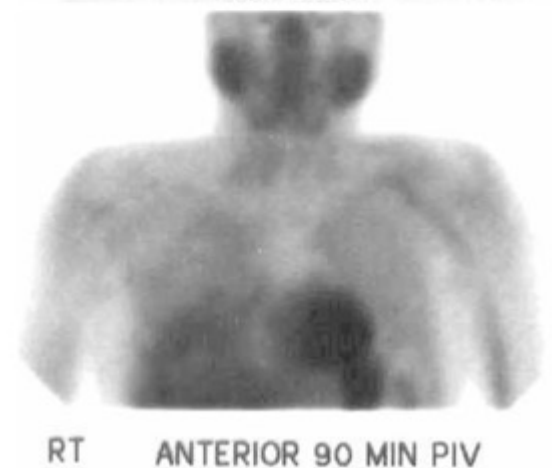
	Sensitivity	Specificity
Pertechnetate/Thallium	73%	94%
CT	68%	92%
US	55%	95%
MRI	50%	87%

Krubsack AJ, Wilson SD, Lawson TL et al. Prospective comparison of radionuclide, computed tomographic, sonographic, and magnetic resonance localization of parathyroid tumors.

Scan of Tc-99m MIBI

Tc-99m MIBI

Heart
GI
Kidney
Bladder



Normal uptake for Tc-99m MIBI

Salivary gland

Parotid gland

Renal

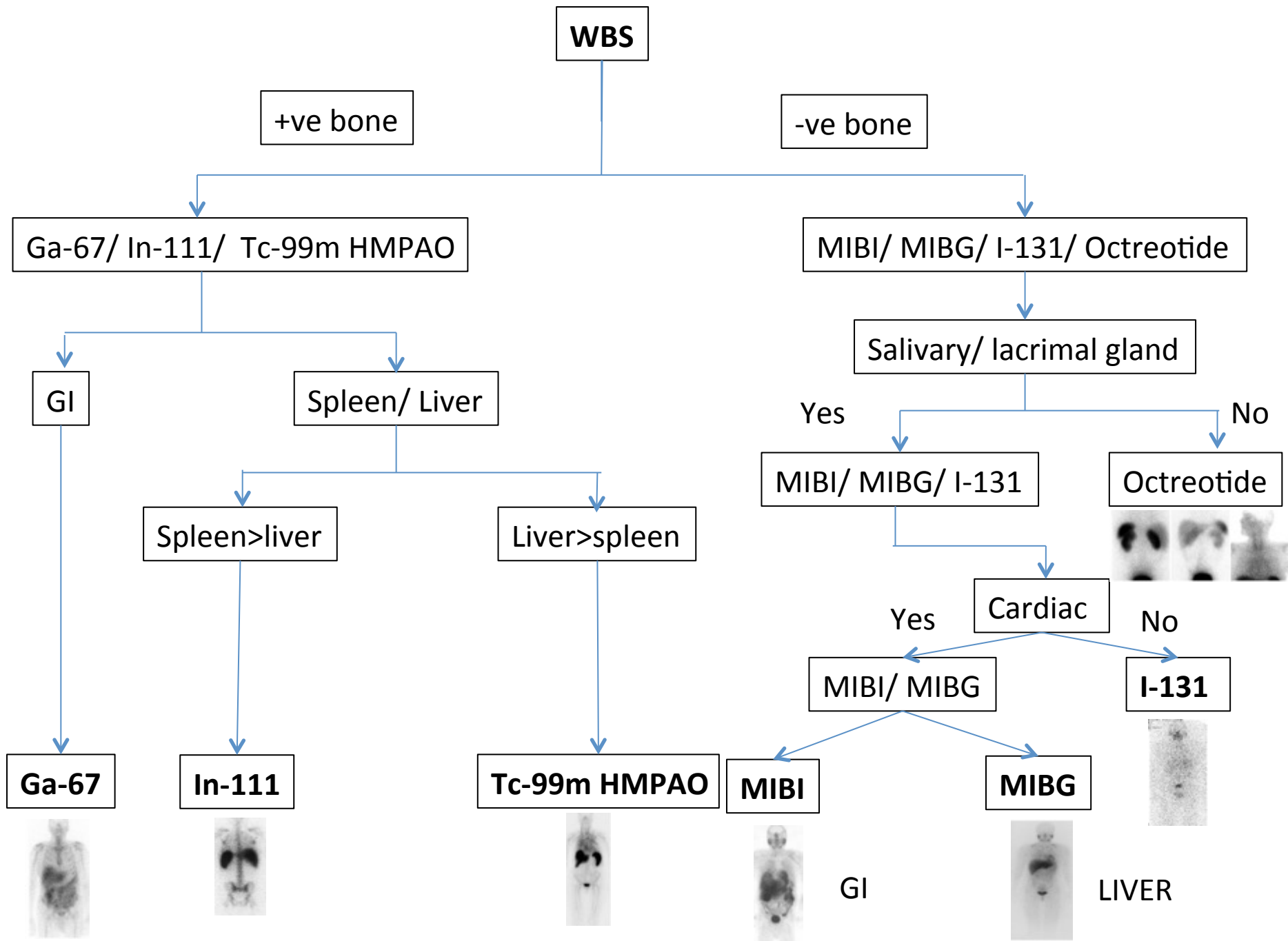
Bladder

Heart

Intestine

Thyroid

Parathyroid



Concerning imaging of parathyroid glands

- A. Approximately 50% of cases of primary hyperparathyroidism are due to a single functioning adenoma
- B. The sensitivity of parathyroid scintigraphy in the detection of adenomas within the gland approaches 75%
- C. In secondary hyperparathyroidism approximately 80% of hyperplastic glands will be visualized
- D. The majority of parathyroid adenomas are functioning
- E. False positive scans may occur in the presence of coexisting thyroid disease

Concerning imaging of parathyroid glands

A. F

B. T

C. F

D. T

E. T

Tc-99m sestamibi uptake may be
found in

- A. Parathyroid hyperplasia
- B. Parathyroid adenoma
- C. Thyroid adenoma

Tc-99m sestamibi uptake may be
found in

A. T

B. T

C. T

In performing Tl-201/Tc-99m
pertechnitate parathyroid studies, it is
best perform the pertechnitate study
first

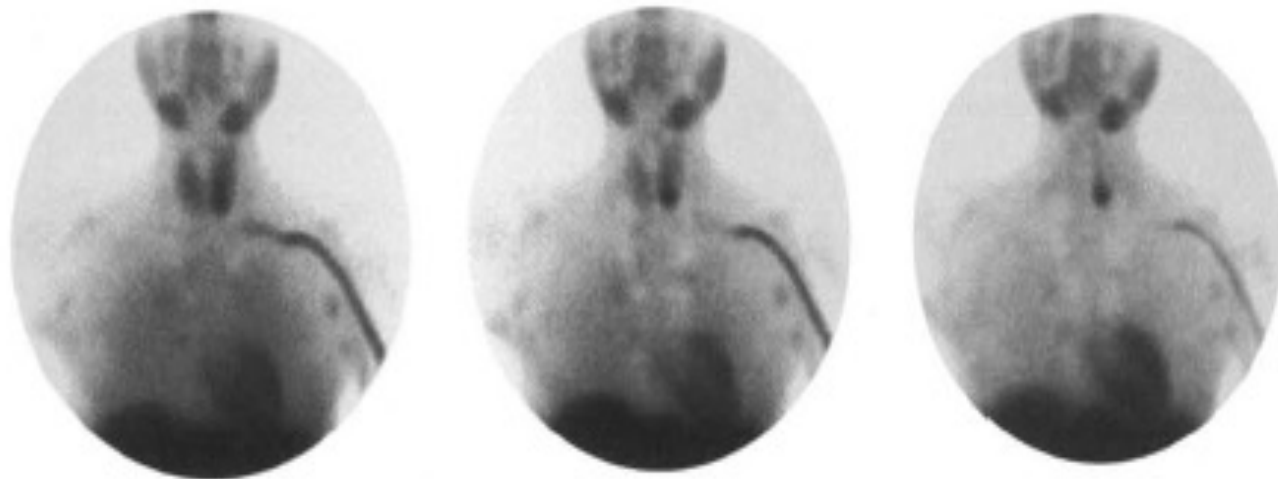
In performing Tl-201/Tc-99m
pertechnitate parathyroid studies, it is
best perform the pertechnitate study
first

- FALSE

What is the typical finding of parathyroid adenomas on parathyroid imaging with Tc-99m sestamibi?

What is the typical finding of parathyroid adenomas on parathyroid imaging with Tc-99m sestamibi?

- Parathyroid adenomas show delayed washout compared with normal thyroid tissue



A 55-year-old man with hypercalcemia has an elevated serum PTH level. Images are taken at 5 minutes and at 1 and 2 hours.

1. Which radiopharmaceutical is being used, and what is the rationale for this technique?
2. What is the diagnosis?
3. What is the accuracy of this study?
4. What is the most common cause for a false-positive study result?

Hyperparathyroidism

1. Tc-99m sestamibi is taken up by thyroid and parathyroid tissue, but wash out more rapidly from the thyroid.
2. Parathyroid adenoma in the region of the left lower lobe of the thyroid.
3. > 90% predictive value for preoperative localization of parathyroid adenoma, lower test accuracy for hyperplasia and small tumors.
4. Thyroid follicular adenoma.

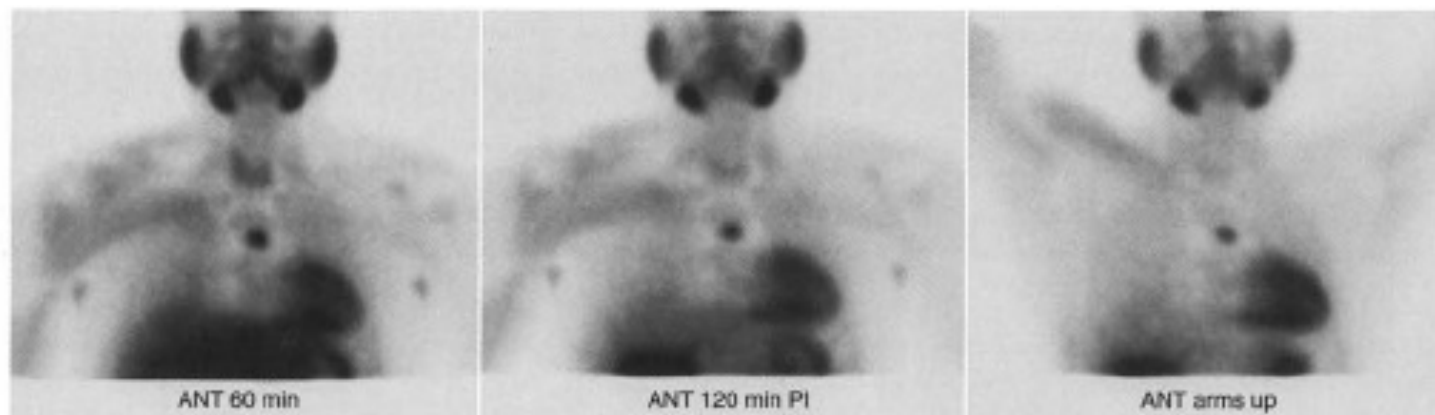


A patient has elevated serum calcium and parathyroid hormone levels and normal findings on neck examination.

1. What other protocol in addition to dual-phase (early and delayed) ^{99m}Tc sestamibi imaging can be used to evaluate for parathyroid disease?
2. Describe how that procedure is performed.
3. Describe the findings. Left: ^{99m}Tc sestamibi; middle: ^{123}I ; right: subtraction.
4. List the differential diagnosis and the most likely diagnosis.

Parathyroid adenoma

1. Dual isotope imaging with subtraction, in the past using Tl-201 and Tc-99m pertechnetate and recently using I-123 and Tc-99m sestamibi
2. I-123 by mouth. After a delay of 2 to 3 hours, an anterior I-123 thyroid scan is obtained. Without moving the patient, an image is obtained after IV injection of Tc-99m MIBI. The I-123 image is computer subtracted from the Tc-99m MIBI image.
3. The I-123 thyroid scan appears normal, although the left lobe extends more inferiorly. The MIBI image shows an asymmetrical bulbous configuration in the region of the right lower pole of the thyroid. Subtraction demonstrates focal radiotracer compatible with parathyroid adenoma at the lower pole of the right thyroid.
4. Parathyroid, thyroid adenoma, thyroid carcinoma and metastatic carcinoma.



A 45-year-old man had surgery for hyperparathyroidism that has persisted postoperatively.

1. What is the radiopharmaceutical and study?
2. Describe the scintigraphic findings.
3. What is the differential diagnosis for these findings?
4. What is the likely diagnosis in this clinical setting?

Mediastinal parathyroid adenoma

1. Parathyroid scan with Tc-99m sestamibi or Tc-99m tetrofosmin.
2. Focal persistent uptake in the mediastinum, normal salivary, liver, cardiac uptake. Axillary uptake resolves with arm elevated, thus is caused by skin folds.
3. Various benign and malignant neoplasm.
4. Mediastinal parathyroid adenoma.

ADRENAL SCINTIGRAPHY

Pearls & Pitfalls

Adrenocortical imaging

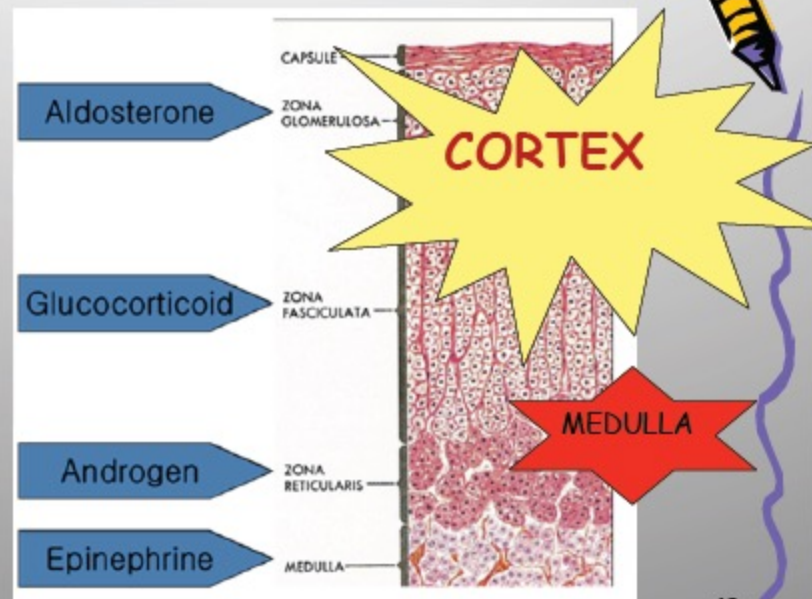
- NP-59 is an adrenal cortical imaging agent with imaging performed at 4-5 days. Unilateral adrenal uptake is usually an adenoma and bilateral uptake is usually due to adrenal hyperplasia

ADRENAL SCINTIGRAPHY

- Common indication is hypercortisolism (Cushing's syndrome)
- Less common :
 - a) Hyperaldosterolism (Conn's syndrome)
 - b) Adrenal virilizing tumors

ADRENAL GLAND

ADRENAL GLAND



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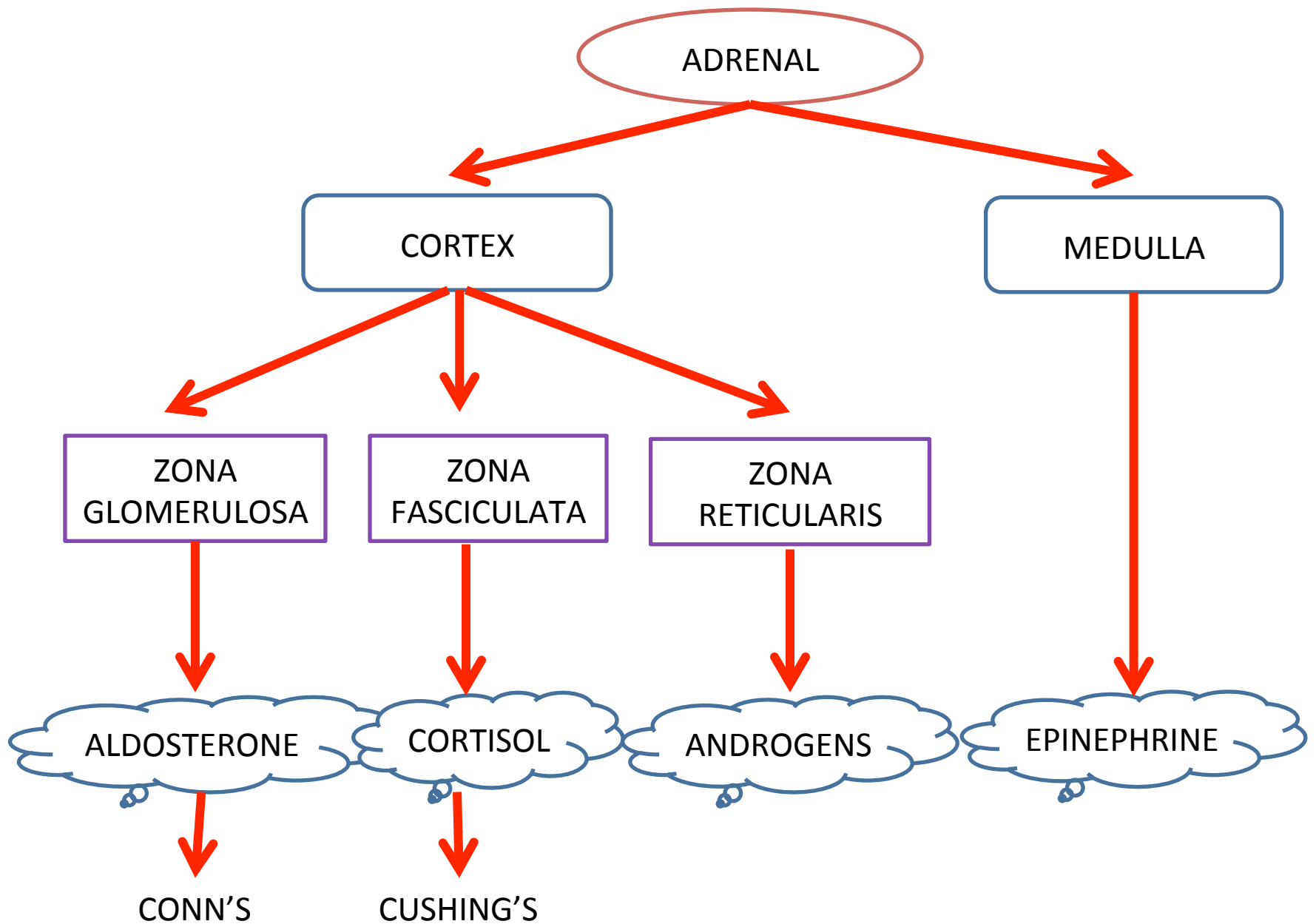
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Epinephrine

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Primary aldosteronism
adenoma
hyperplasia

Aldosterone

Cushing syndrome
adenoma
adenocarcinoma
hyperplasia
ACTH-dependent
ACTH-independent

Glucocorticoid

Pheochromocytoma
extraadrenal

Epinephrine

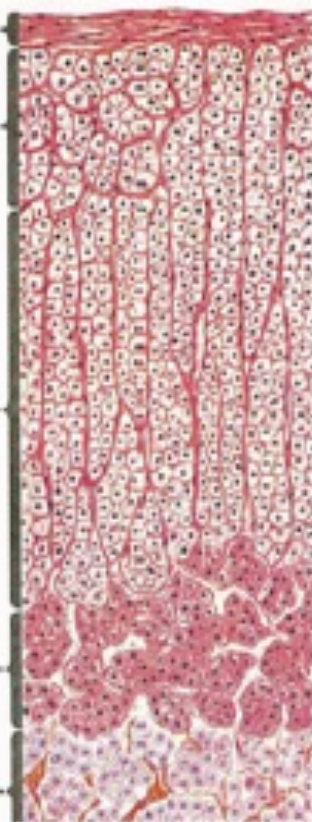
CAPSULE

ZONA
GLOMERULOSA

ZONA
FASCICULATA

ZONA
RETICULARIS

MEDULLA



Radiopharmaceutical - 1

- ^{131}I -6 β -19-norcholesterol
 - Cholesterol analog
 - Incorporated in LDL (low density lipoproteins)
 - Slow intravenous administration with elimination is intestinal with enterohepatic cycle.
 - Accumulates in the adrenal cortex , esterified but NOT metabolized



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Drugs that interfere with NP – 59 uptake

Drug	Mechanism
Spironolactone	Aldosterone receptor blocker
Ketoconazole	Suppression of cortical biosynthesis
Diuretic/oral contraception	Stimulate renin/angiotensin
Glucocorticoids	Suppression of ACTH
Cholesterol lowering agents	Decrease cholesterol
Hypercholesterolemia	Decrease LDL receptor activity

PROTOCOL & TECHNIQUES



Before

- Thyroid saturation (hrs before → 7 days_
- 100 mg stable iodide /day eg Lugol's

STOP

- Stop all the medications that may interfere with the uptake

+/-

- Dexamethasone suppression (4mg/QID 7days prior to injection, till last acquisition)

NP-59

- 20-40 MBq slow intravenous injection

IMAGING

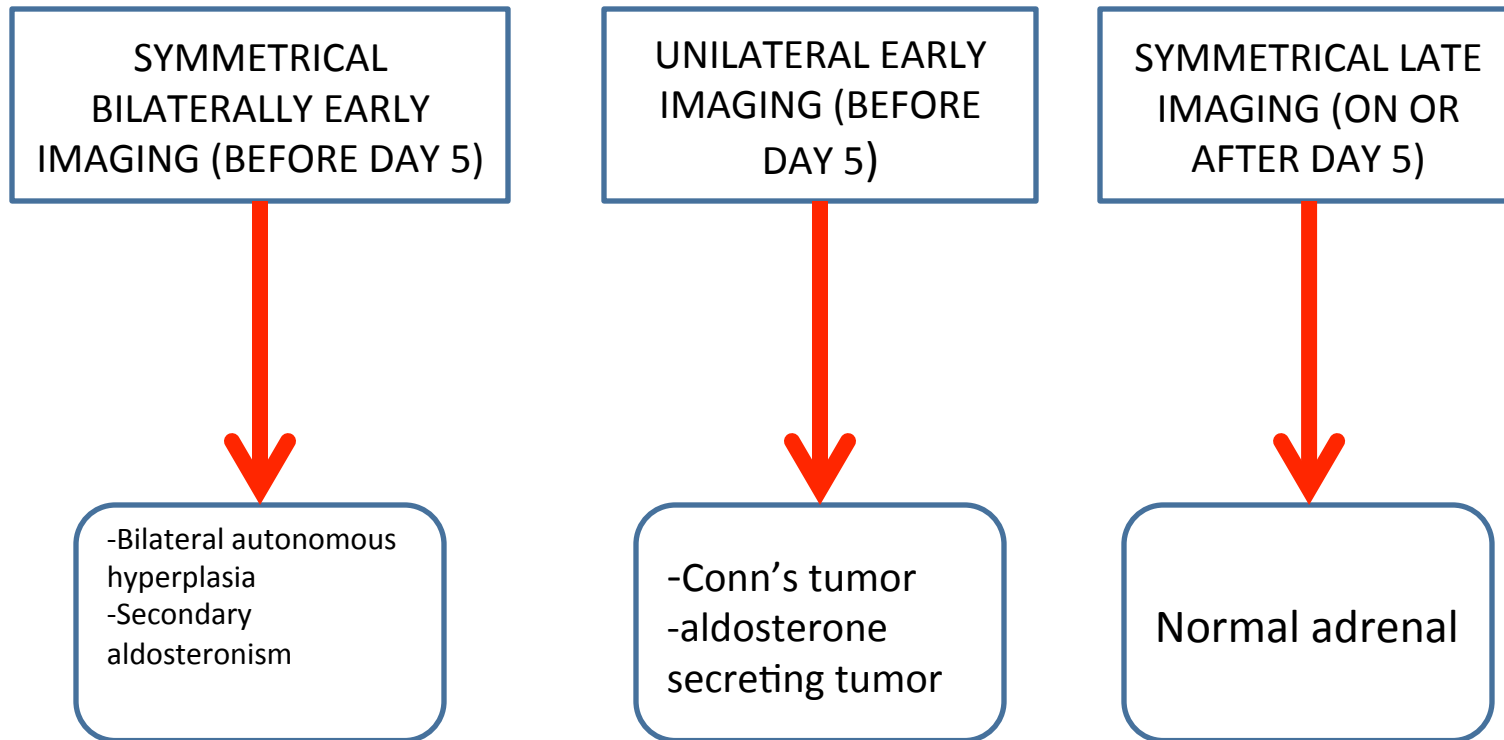
- At D2-up to D10



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HYPERALDOSTERONISM NP-59 PATTERN

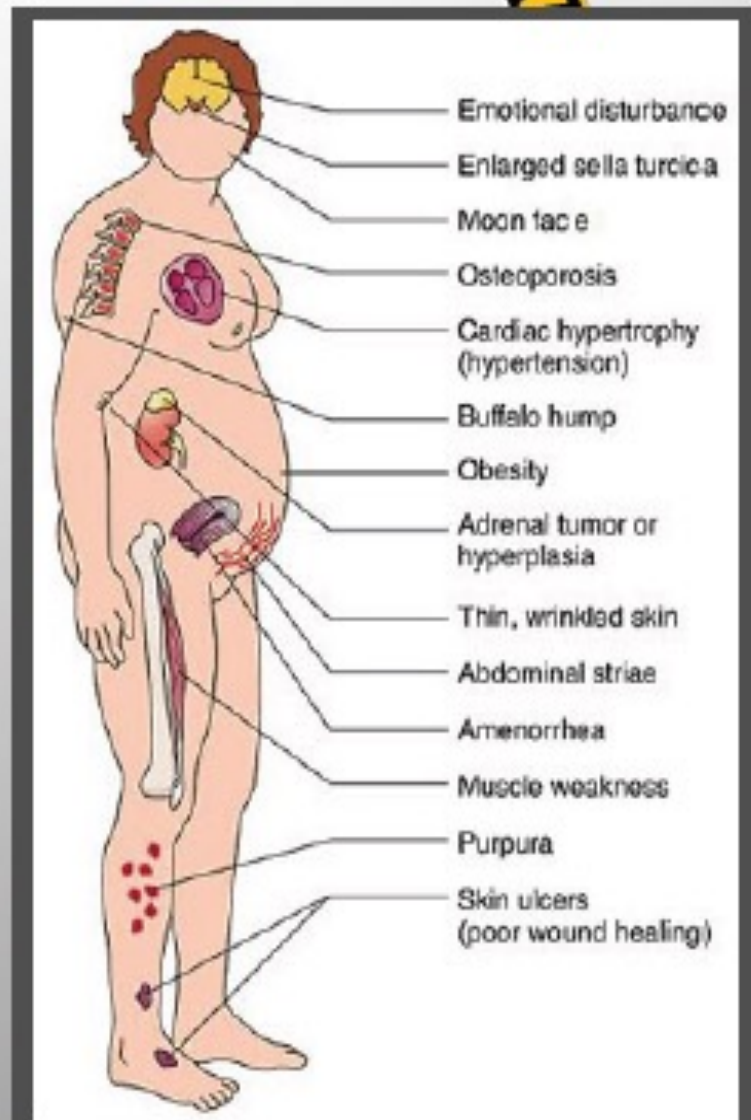


Cushing Syndrome-1

- Either ACTH dependent
- Non ACTH dependent



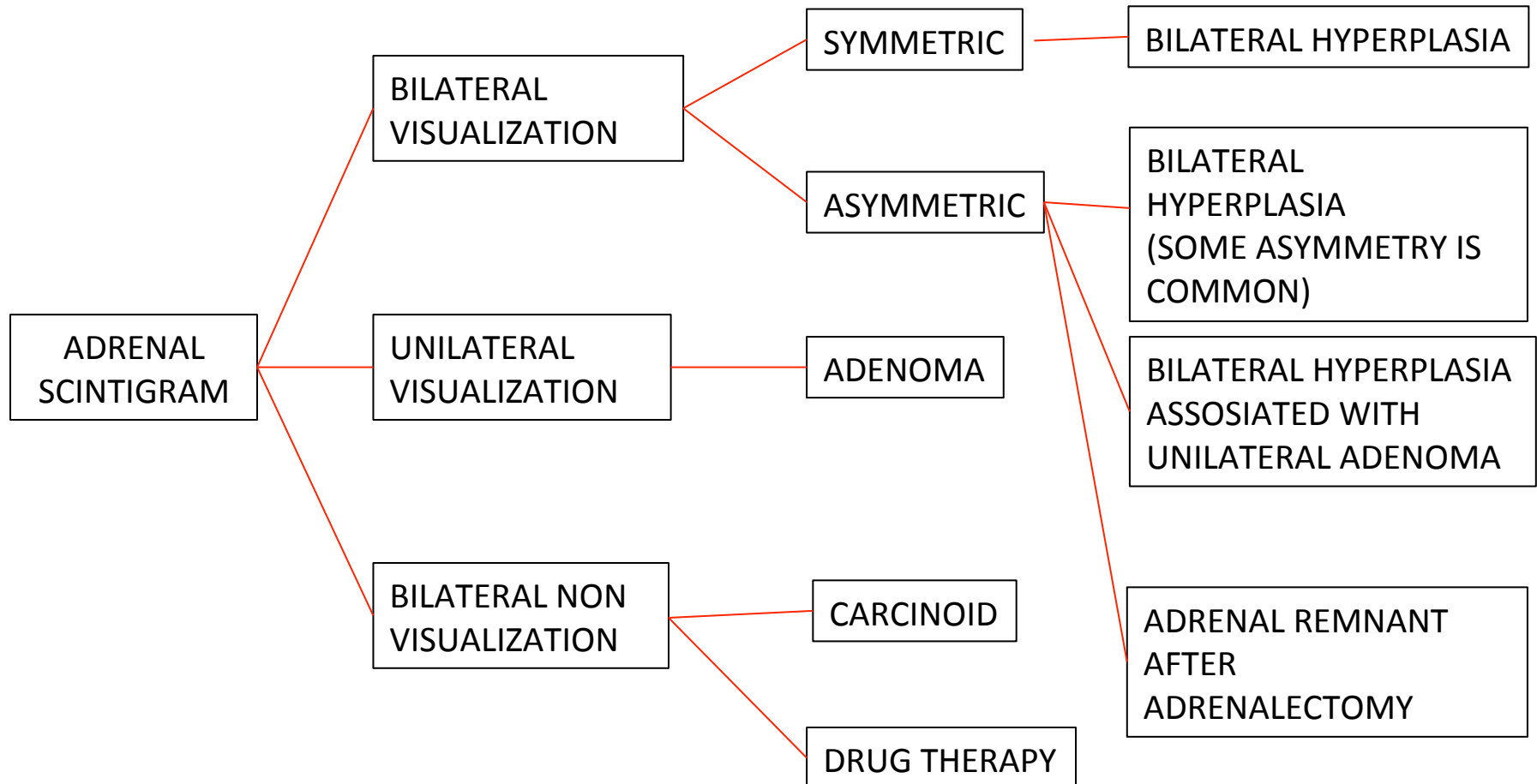
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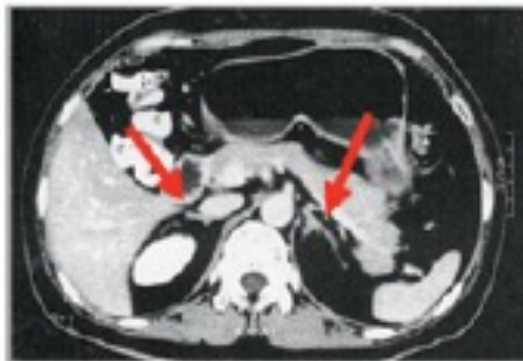
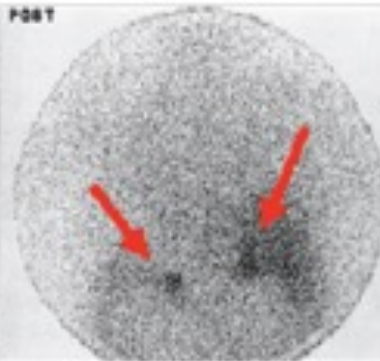
Clinical manifestations of Cushing's syndrome.
Source: Emanuel Rubin, John L. Farber, *Pathology*,
3rd edition, Lippincott-Raven Publishers (1999)

CUSHING'S SYNDROME NP-59

PATTERN



Cushing Syndrome -2



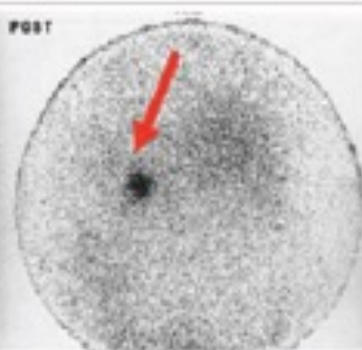
Bilateral adrenal
hyperplasia

The scintigraphic pattern of ACTH-dependent Cushing syndrome :

symmetric to varying degrees of asymmetric,
bilateral visualization of the adrenal glands on NP-59 imaging



Cushing Syndrome -3

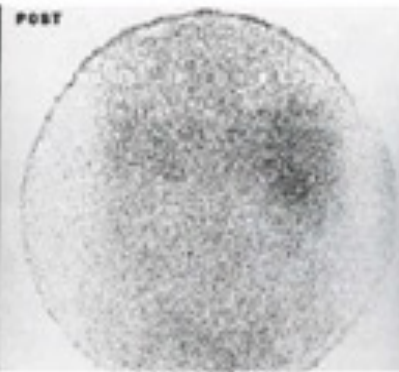


Lt adrenal
adenoma

The scintigraphic pattern of adrenal adenoma :
unilateral visualization of the gland containing
the adenoma;
the contralateral gland is not visualized



Cushing Syndrome - 4



Lt adrenal
adenocarcinoma

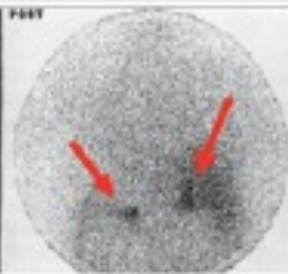
- In adrenal carcinoma, there is nonvisualization of the adrenal glands bilaterally.



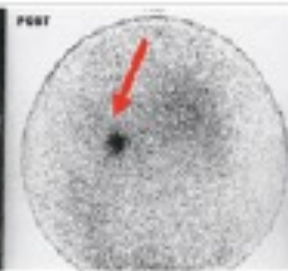
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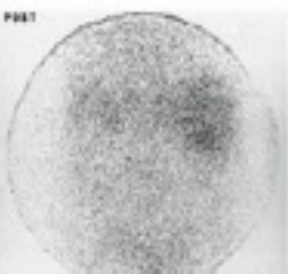
Cushing Syndrome -6



Bilateral adrenal
hyperplasia



Lt adrenal
adenoma



Lt adrenal
adenocarcinoma



Hyperandrogenism (Virilization) -1

- Done in conjunction with dexamethasone suppression



Hyperandrogenism (Virilization) -2

- Results:

Early bilateral visualization (<5 days)	Bilateral zona reticularis adrenal hyperplasia
Early unilateral/ marked asymmetric adrenal visualization	Adrenal adenomas
Bilateral late visualization (>5 days)	Normal



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Problems

- Significant high radiation burden**
- Requires patient's preparation which may cause serious adverse events esp in those with hyperaldosteronism (hypertensive crisis)
- ALTERNATIVE 18F-FDG PET-CT



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Concerning scintigraphy of the adrenal

- A. Asymmetrical uptake of NP 59 may be seen in two thirds in normal subject
- B. Bilateral symmetrical uptake of NP 59 in the presence of glucocorticoid excess is usually due to adrenal hyperplasia
- C. Unilateral increased uptake following NP 59 is most commonly due to functioning adenoma
- D. Bilateral non visualization of the adrenals in the presence of endogenous glucocorticoid excess is most likely to be due to adrenal carcinoma
- E. Unilateral non visualization exclude an adrenal carcinoma

Concerning scintigraphy of the adrenal

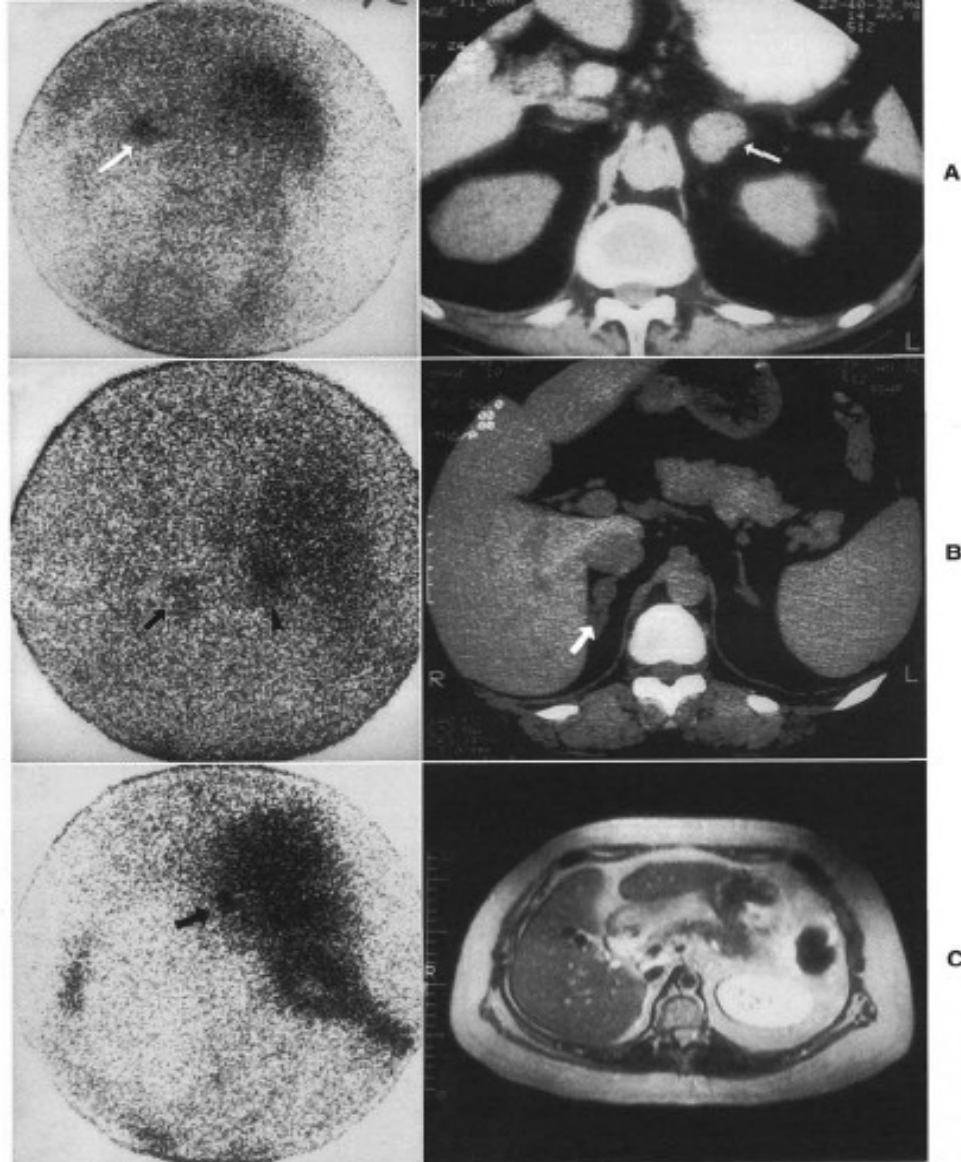
- TTTTF

In the scintigraphy assessment of adrenal hypertension

- A. Pretreatment with dexamethasone in patients with primary hyperaldosteronism significantly improves the diagnostic accuracy of NP 59 scanning
- B. Following dexamethasone suppression, a Conn's adenoma will usually be seen before day five
- C. NP 59 scintigraphy can distinguish ACTH dependent from ACTH independent Cushing's syndrome
- D. False negative results may be seen during MIBG scanning in patients with pheochromocytoma on steroid therapy
- E. Activity in the normal gland is usually suppressed in the presence of a unilateral pheochromocytoma

In the scintigraphy assessment of adrenal hypertension

- TTTF



Three patients with Cushing's syndrome were referred for an ^{131}I iodocholesterol study (NP-59). CT and NP-59 (*posterior views*) studies are shown. Arrows are a bonus.

1. Patients *A* and *B* have a similar history of newly diagnosed hypercortisolism. Describe the findings and give interpretations.
2. Patient *C* had previous adrenalectomy for Cushing's syndrome but continues to have hypercortisolism. Describe the findings and give an interpretation.
3. What is the mechanism of uptake of the radiopharmaceutical?
4. What other diseases besides Cushing's syndrome can be diagnosed with NP-59?

Adrenocortical scintigraphy

1. A, Unilateral NP-59 uptake consistent with left adrenal adenoma, concordant with the CT. B, Bilateral adrenal hyperplasia, discordant with CT.
2. Uptake in the right adrenal bed region indicating adrenal remnant. Discordant with the negative CT.
3. Transport and receptors system for serum cholesterol account for adrenal uptake. Cholesterol is required for the production of adrenal hormones.
4. Hyperaldosteronism (adrenal adenoma or hyperplasia) and hyperandrogenism.

ADRENOMEDULLARY SCINTIGRAPHY

Pearls & Pitfalls

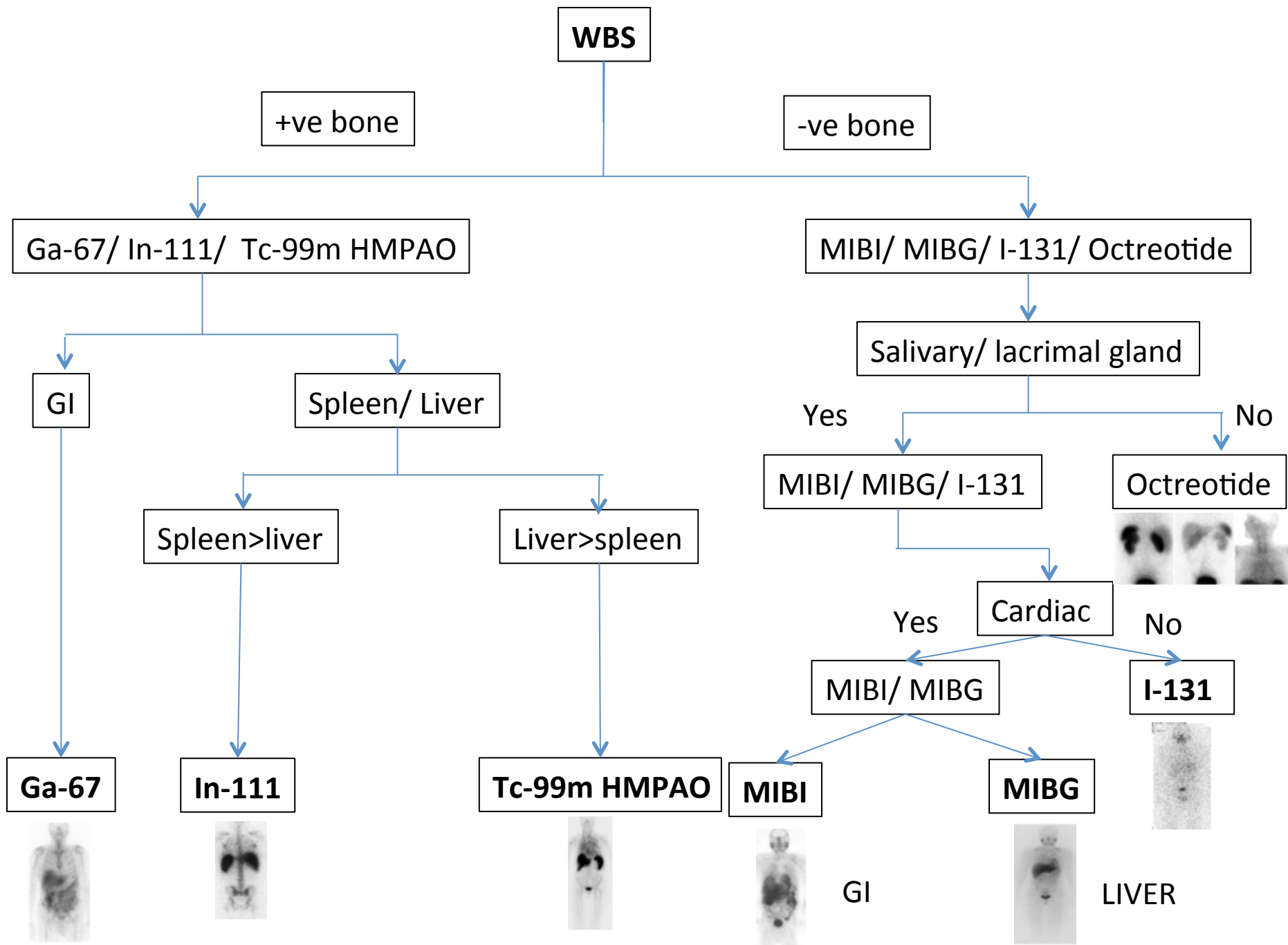
Adrenomedullary imaging

- MIBG is a medullary adrenal imaging agent which effectively localizes in pheochromocytoma and neuroblastoma. It may also localize in carcinoid, medullary thyroid carcinoma and paraganglioma.

- MIBG → phaeochromocytoma, neuroblastoma
- Octreotide scan → paraganglioma, carcinoid
- PET-CT for better resolution and anatomical localization



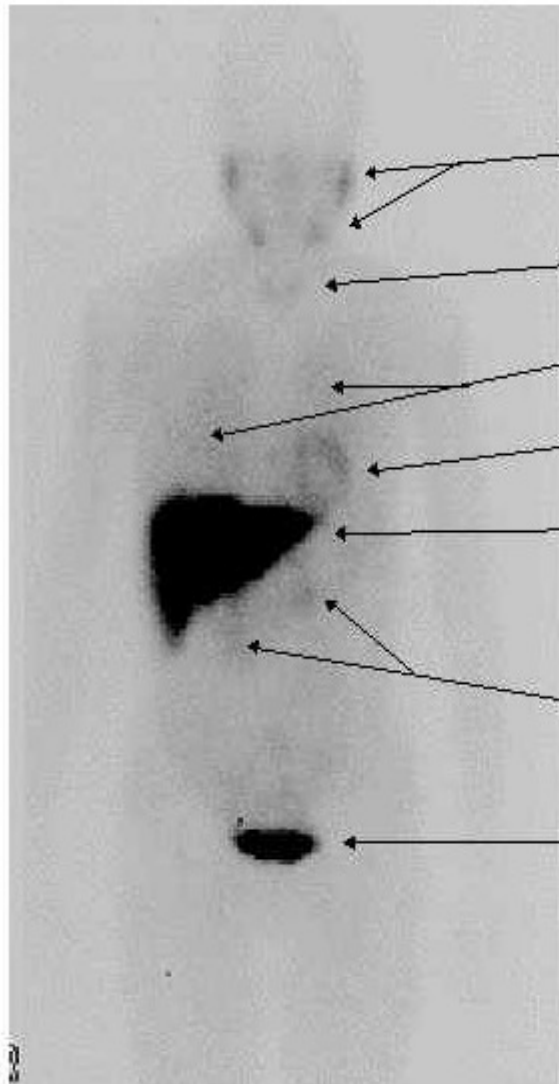
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Front View

Two Examples of Adrenal mIBG Scans

Back View



Example 1

Salivary
Glands

Thyroid

Lungs

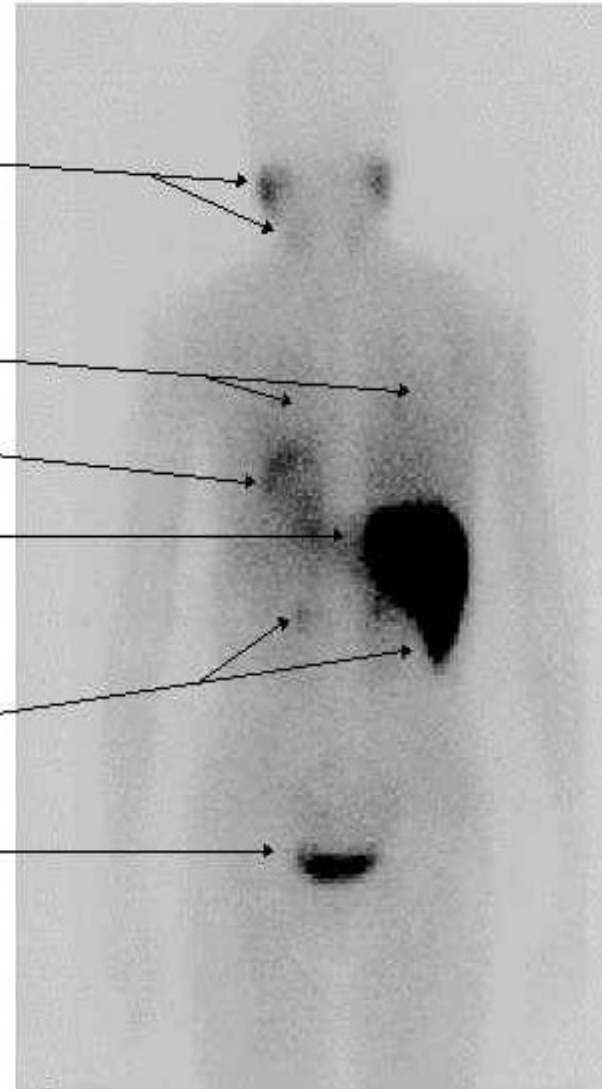
Heart

Liver

Kidneys

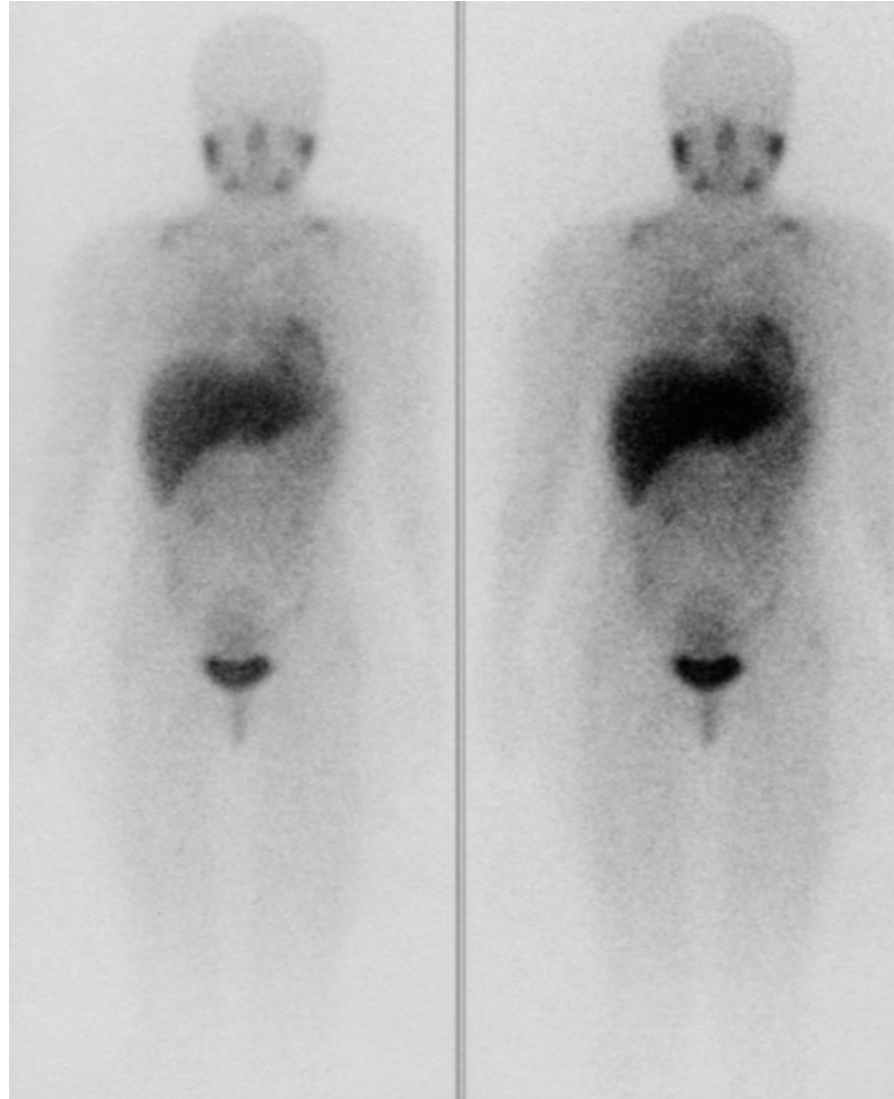
Bladder

This scan is
normal



Heart
Liver
Kidney
Bladder

MIBG scan



Heart
Liver
Kidney
Bladder

Radiopharmaceutical MIBG-1

- Metaiodobenzylguanidine (MIBG)
 - Guanethidine analog
 - Structurally similar to norepinephrine.
 - Type I uptake mechanism and stored in the catecholamine storage vesicles
 - To image the adrenal medulla and sympathomimetic tissues
 - Abnormal localization :
phaeochromocytomas, neuroblastomas.



MIBG- TECHNIQUE

- Prior to administration.
 - Thyroid blockade with potassium iodide
 - Withhold some medications that may interfere with the MIBG uptake
- Slow* intravenous injection (at least 5 minutes)
- Imaging time depends on types I-123 or I-131



Thyroid blockade

- Potassium perchlorate for emergency and allergic to iodine= 400 mg

Compound	Daily dose
Capsules	
Potassium iodate	170 mg
Potassium iodide	130 mg
Solution	
Lugol 1%	1 drop/kg max 40 (20 drops bd)

Drugs that interfere with MIBG uptake

Mechanism of Interference	Drugs	Suggested Period of Withdrawal (Days)
Inhibition of uptake-1	Cocaine, opioids	7-14
	Tricyclic antidepressants (amitriptyline and derivatives, imipramine and derivatives, amoxapine, loxapine, doxepine, others)	7-21
	Antipsychotics (phenothiazines,* thiozanthines, butyrophenones)	21-28
	Labetalol, metoprolol	21
Inhibition of granular uptake	Reserpine, tetrabenazine, etc	14
Competition for granular uptake	Norepinephrine, serotonin, guanethidine, etc	14
Depletion of storage granules	Reserpine, guanethidine, labetalol, etc	14-21
	Sympathomimetics† (such as phenylpropanol-amine, amphetamine, dopamine, isoproterenol, salbutamol, etc)	
Increased uptake and retention	Calcium channel blockers	14
	Angiotensin-converting enzyme inhibitors	14

- 
- 87% sensitivity and 99% specificity for detection of pheochromocytomas.
 - 91% sensitive in detecting neuroblastoma
 - Lesser sensitivity in detecting carcinoid and medullary thyroid carcinoma*



12/28/11

Somatostatin analogues-1

INDICATIONS

- Imaging of :
 - Paragangliomas
 - Carcinoids
 - Neuroblastomas
- Sensitivity in phaeochromocytomas is inferior to MIBG (25%), but better for paragangliomas (80%) esp in H& N
- 5 subtypes (SSR1 to 5)



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1. The pathophysiologic basis of nuclear medicine; Springer 2006

2. Radionuclide imaging of phaeochromocytoma and paraganglioma. Imaging, Volume 3, Issue 72, Dec 2008

Somatostatin analogues-2

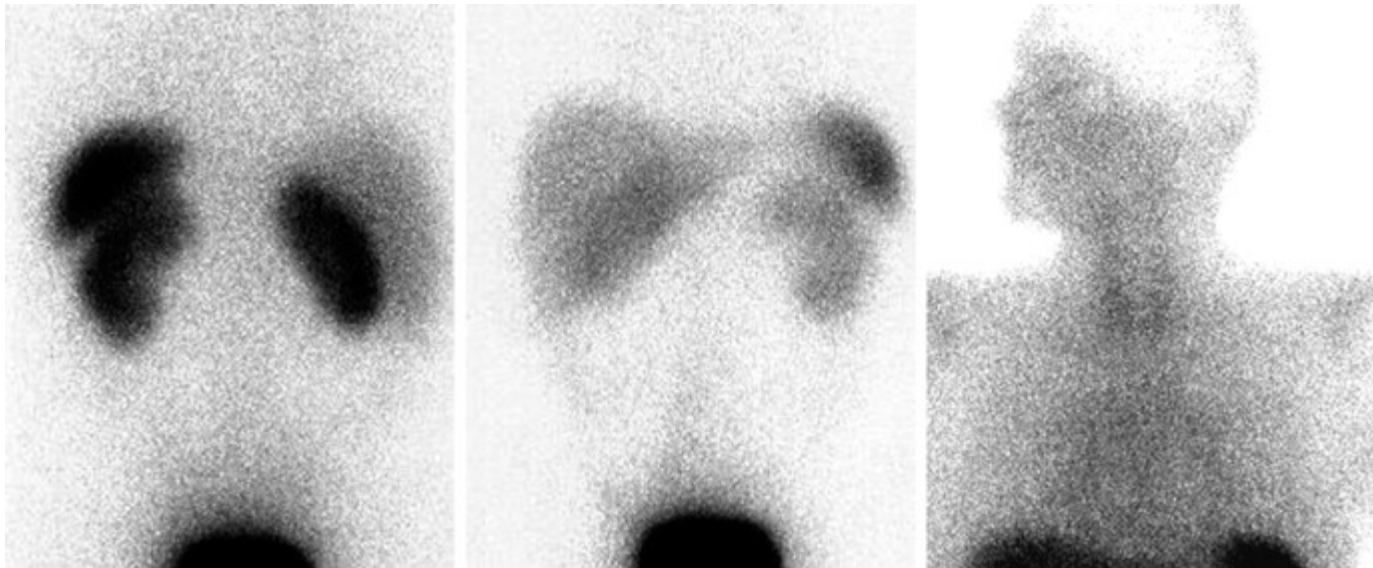
RADIOPHARMACEUTICAL

- Indium -111 Octreotide (Octreoscan)
 - Strong affinity for subtype 2 and 5.
- Preparation:
 - Withhold octreotide therapy
- Static images at 4H and 24H post intravenous injection of 6 mCi



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In-111 pentetreotide (octreoscan)
normal uptake at kidney, spleen, liver ,
thyroid and intestinal activity



Somatostatin analog limitations

False negative

Small &

Few somatostatin receptors

POSITRON EMITTING RADIONUCLIDES

- ^{11}C -epinephrine
- ^{11}C -hydroxyepinephrine
- ^{18}F -fluorodihydroxyphenylalanine (^{18}F -DOPA)
- ^{18}F -fluorodopamine (^{18}F -DA)
- ^{18}F -FDG



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Positron Emission Tomography-1

- ^{18}F -FDG :
 - The only PET-CT imaging agent that is widely available
 - Not specific*
 - 70% sensitivity
 - Alternative in MIBG negative



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PET-2



- 18F-DOPA & 18F-DA
 - Excellent imaging of paraganglioma and phaeochromocytomas
 - Sensitivity is superior to FDG
 - 18F-DA overall sensitivity in detecting phaeochromocytoma of 90%, MIBG (76%), SRS (22%)
 - Specificity is similar to MIBG
 - Easy interpretation*
 - Easy patient's preparation**
- Limited by high cost



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Multiple endocrine neoplasia (MEN) type 1

- Dominantly inherited
- Mutation of MEN 1 gene on chromosomal region 11q13
- Include :
 - ✓ Parathyroid = hyperplasia or adenoma (90%)
 - ✓ Pancreatic islet = adenoma, carcinoma or hyperplasia (80%)
 - ✓ Anterior pituitary = adenoma (65%)
 - ✓ Adrenal cortex = hyperplasia or adenoma (40%)
 - ✓ Carcinoid tumors and lipomata

Multiple endocrine neoplasia (MEN) type 2

- Parafollicular cells of thyroid = Medullary carcinoma (> 95%)
- Adrenal gland = pheochromocytoma (50%)
- Parathyroid = hyperplasia or adenoma (<25%)

Box 9-8 Multiple Endocrine Neoplasia (MEN) Syndromes

LESION	MEN-I	MEN-IIA	MEN-IIB
Pituitary adenoma	+		
Pancreatic islet cell tumor	+		
Parathyroid adenoma	+	+	
Pheochromocytoma		+	+
Medullary thyroid cancer		+	+
Ganglioneuroma			+

The following tissues may show increased uptake of MIBG

- A. Non-secreting paraganglioma
- B. Small (oat) cell bronchogenic carcinoma
- C. Squamous carcinoma of the bladder
- D. Medullary carcinoma of the thyroid
- E. The heart

The following tissues may show increased uptake of MIBG

- TTFTT

The following are true concerning MIBG scanning

- A. Focal bone marrow activity in the presence of a known neuroblastoma may be normal
- B. The sensitivity of MIBG scanning in the detection of neuroblastoma is approximately 90%
- C. MIBG scanning is more accurate than CT or MRI in the detection of primary adrenal pheochromocytoma
- D. Increased adrenal uptake of MIBG in the MEN syndrome confirm the presence of pheochromocytoma
- E. MIBG scanning accurately reflects the extent of bony involvement in metastatic neuroblastoma

The following are true concerning MIBG scanning

- FTFFF

A. I-131 NP 59

B. In-111-Octreoscan

C. I-131 MIBG

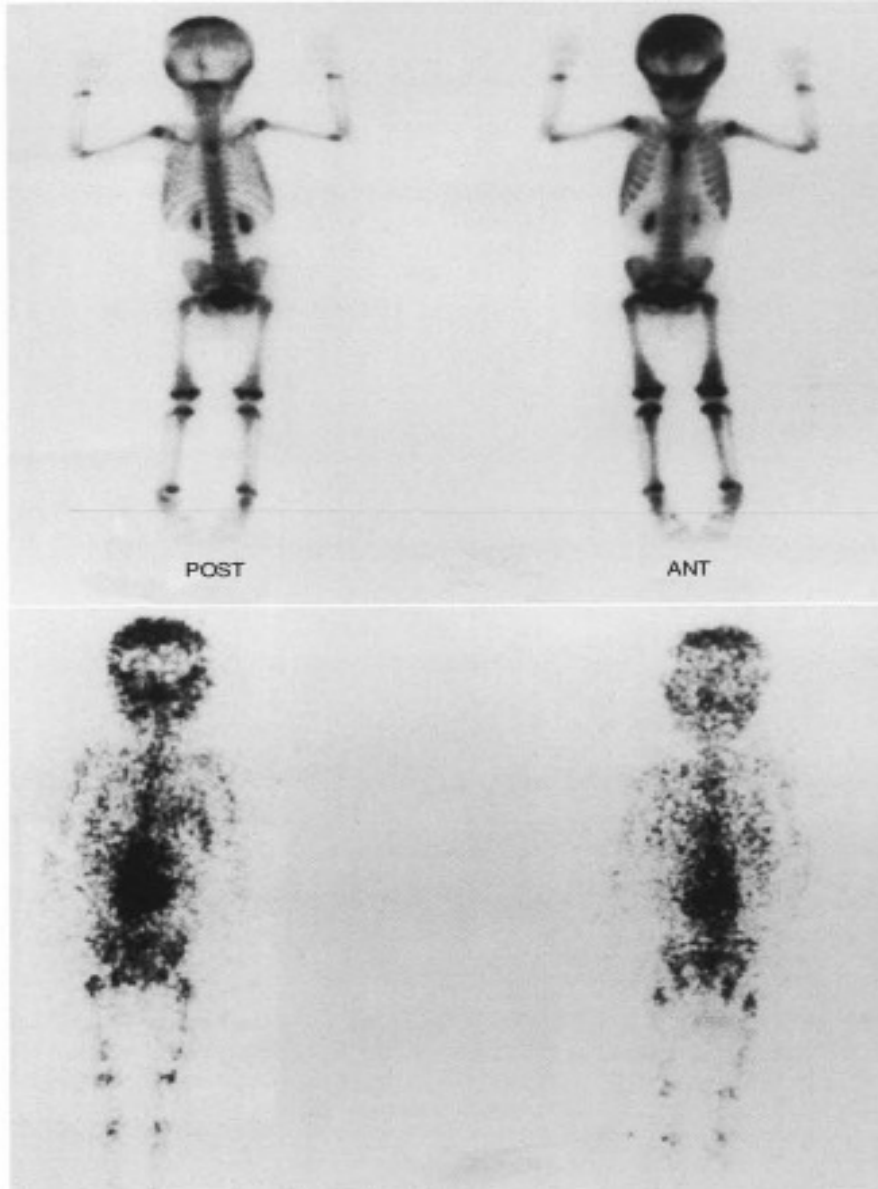
1. Adrenal cortical adenoma
2. Pituitary adenoma
3. Medullary thyroid carcinoma
4. Pheochromocytoma
5. Carcinoid tumor

A. I-131 NP 59

B. In-111-Octreoscan

C. I-131 MIBG

1. Adrenal cortical adenoma = A
2. Pituitary adenoma = B
3. Medullary thyroid carcinoma = B
4. Pheochromocytoma = C
5. Carcinoid tumor = B

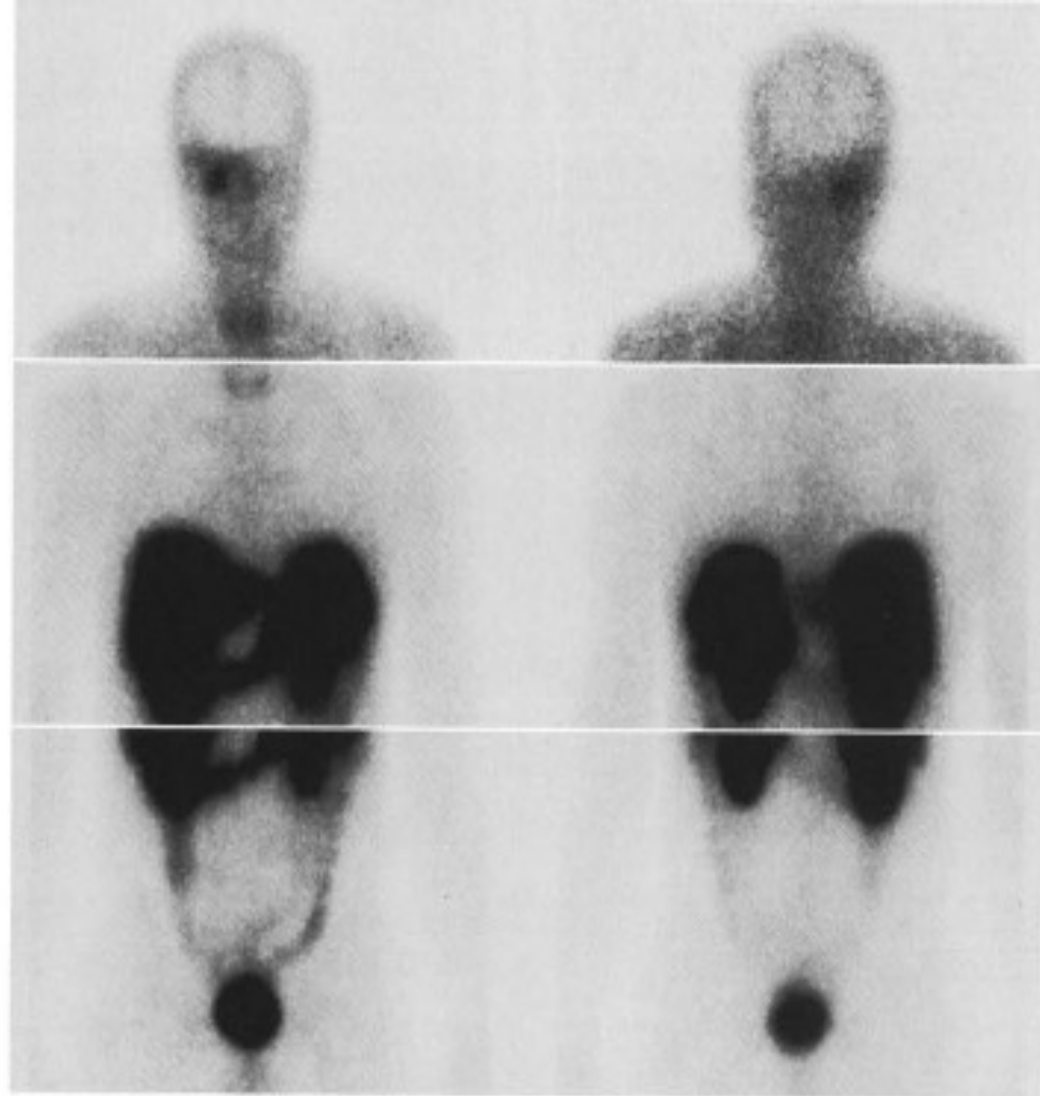


A 3-year-old boy with a recently diagnosed retroperitoneal tumor.

1. Describe the imaging findings of the ^{99m}Tc MDP bone scan (A) and the ^{131}I MIBG study (B).
2. What is your interpretation of the two studies?
3. What are the most common tumor causes for extrasosseous uptake of bone-seeking radiopharmaceuticals in this age group?
4. What is the most sensitive imaging method for detection of bone metastases in this disease?

Neuroblastoma

1. Bone scan shows uptake symmetrically in the distal femurs, cranial and facial bones. I-131 MIBG shows a large area of midline abdominal uptake. Inspection of the bone scan in the same area suggests a soft tissue left perirenal density, best seen in the anterior view. In addition, diffuse marrow/bone uptake is seen on the MIBG study.
2. The prominent mid line uptake on the MIBG is consistent with neuroblastoma. Subtle bone uptake is seen in the region. The symmetrical bone uptake in the distal femurs, cranial and facial bone is very suggestive of tumor. The MIBG confirms metastatic disease with extensive tumor in the marrow/ bone from skull to feet.
3. First, primary neuroblastoma. Osteosarcoma metastatic to the lung is another. Metastases of various tumors occasionally are seen on bone scans, lung, colon and breast.
4. Combination of Tc-99m bone scan and I-131 MIBG.

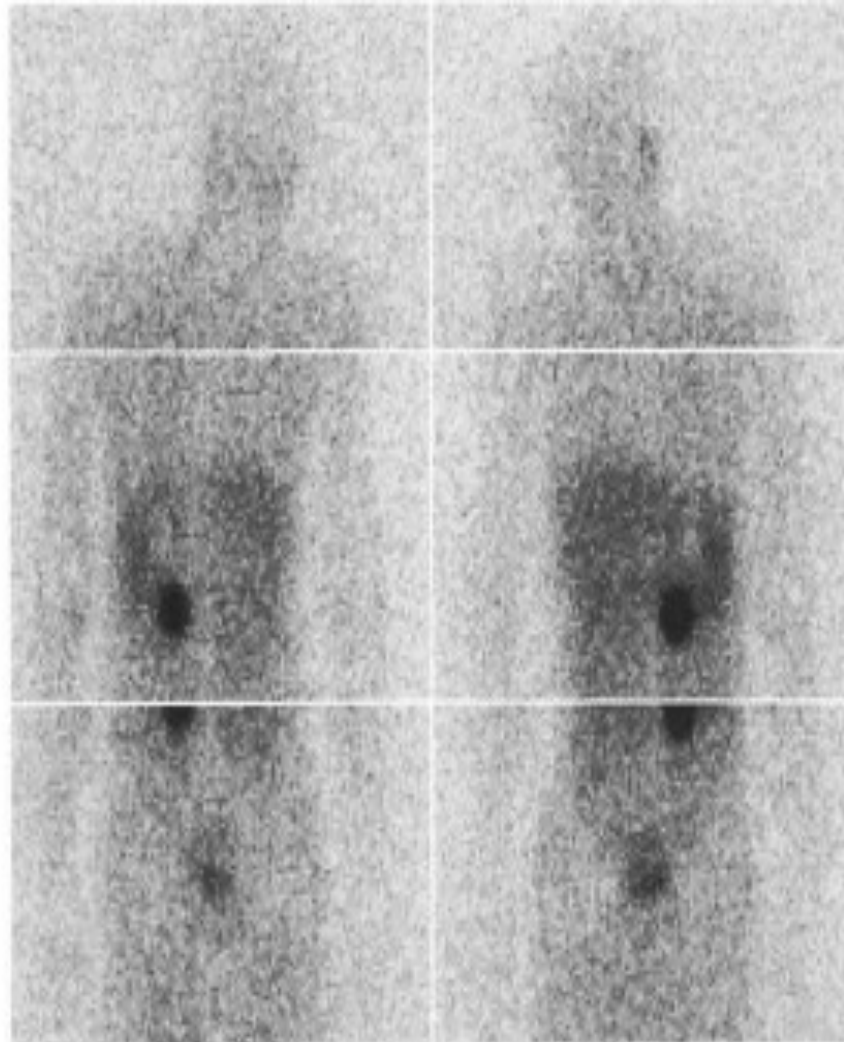


A patient with a neuroendocrine disorder and pulsatile tinnitus in the right ear. CT study shows a mass in the right temporal bone.

1. What radiopharmaceuticals are applicable?
2. Based on the biodistribution, what agent was used?
3. Describe the findings in the head and neck.
4. Provide the most likely diagnosis and a differential diagnosis.

Octreoscan

1. In-111 octreoscan (octreotide), I-131 MIBG.
2. Prominent liver, spleen and kidney uptake is seen with In-111 octreoscan.
3. Focal abnormal uptake in the right temporal bone that correlates with CT.
4. Paraganglioma considering the patient's history, also meningioma or NET metastasis.

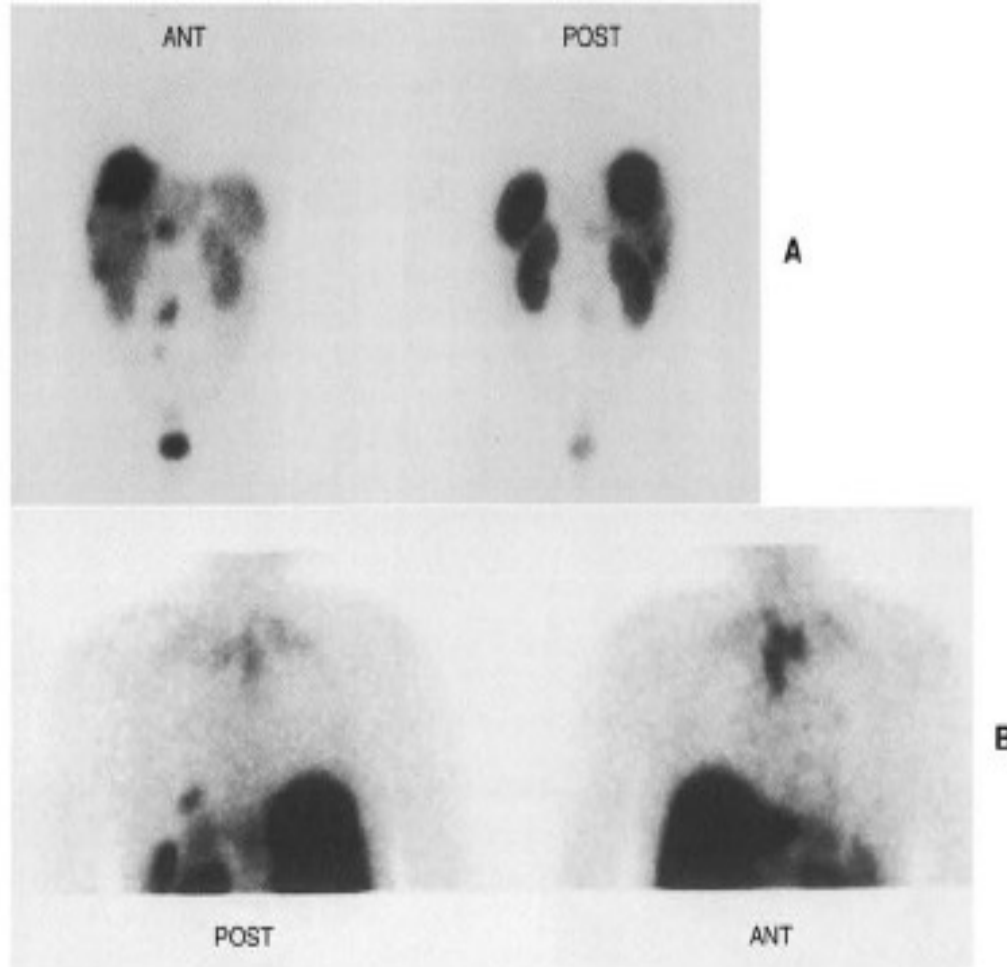


A 47-year-old woman with recent onset of severe hypertension and elevated catecholamine levels.

1. What is the radiopharmaceutical?
2. What is the radiopharmaceutical's mechanism of uptake?
3. What is the accuracy of this study for locating the site of disease? What is the disease?
4. What other diseases take up this radiopharmaceutical?

Pheochromocytoma

1. I-131 MIBG
2. Localization occurs through the norepinephrine reuptake mechanism. It localizes in catecholamine storage vesicles in presynaptic adrenergic nerve ending and cells of the adrenal medulla.
3. Sensitivity: 90%, specificity, 95% for detection of pheochromocytoma.
4. Neuroblastoma (90%), carcinoid (50%) and medullary thyroid carcinoma (25%).



A, 70-year-old man with recent onset of flushing, diarrhea, elevated 5-hydroxyindoleacetic acid (5-HIAA), and a diagnosis of carcinoid syndrome. *B*, 56-year-old patient with past history of medullary carcinoma of the thyroid and recent increase in serum calcitonin levels.

1. Provide the mechanism of uptake of ^{111}In pentetreotide (OctreoScan).
2. List the category of tumors for which this radiopharmaceutical is particularly useful.
3. Describe the image findings on these two studies: *A* (abdominal/pelvis view) and *B* (chest views), and give your interpretation.
4. Name the organs that normally have greatest uptake of the radiopharmaceutical.

NET

1. Peptide analogue of somatostatin and octreotide. Binds to tumors with somatostatin receptors.
2. NET
3. A, multiple metastases to both lobe of the liver. Two large foci and one small focus of uptake consistent with paraaortic tumor adenopathy. Possible small tumor in right hilum. B, prominent irregular uptake in the anterior mediastinum and focal uptake in the lower lung posteriorly.
4. Kidney and spleen.

Infection and inflammation

Pearls & Pitfalls

Infection and inflammation

- Gallium-67 citrate and In-111 leukocyte scans are usually photon poor and the images are coarse or grainy.
- Tc-99m leukocyte scan have more counts and the images appear less grainy and smoother.
- Gallium-67 photon energies are 90, 190, 290 and 390 keV.
- In-111 photon energies are 173 keV and 247 keV.

Pearls & Pitfalls

Infection and inflammation

- Gallium-67 activity is normally seen in the skeleton, lacrimal glands, nasopharynx and liver. Liver activity is usually greater than spleen. Colon activity is normal on delayed images.
- Indium-111 leukocyte activity is normally seen in the bone marrow, liver and spleen with spleen more intense than liver.
- Patchy lung activity may be due to leukocyte damaged during labeling.

Pearls & Pitfalls

Infection and inflammation

- Colonic activity is normal on Ga-67 and Tc-99m leukocyte scans but not on In-111 leukocyte scans.
- Renal activity may be seen normally on Ga-67 images during the 1st 24 hours and on Tc-99m leukocyte images but not on In-111 leukocyte scans.

Pearls & Pitfalls

Infection and inflammation

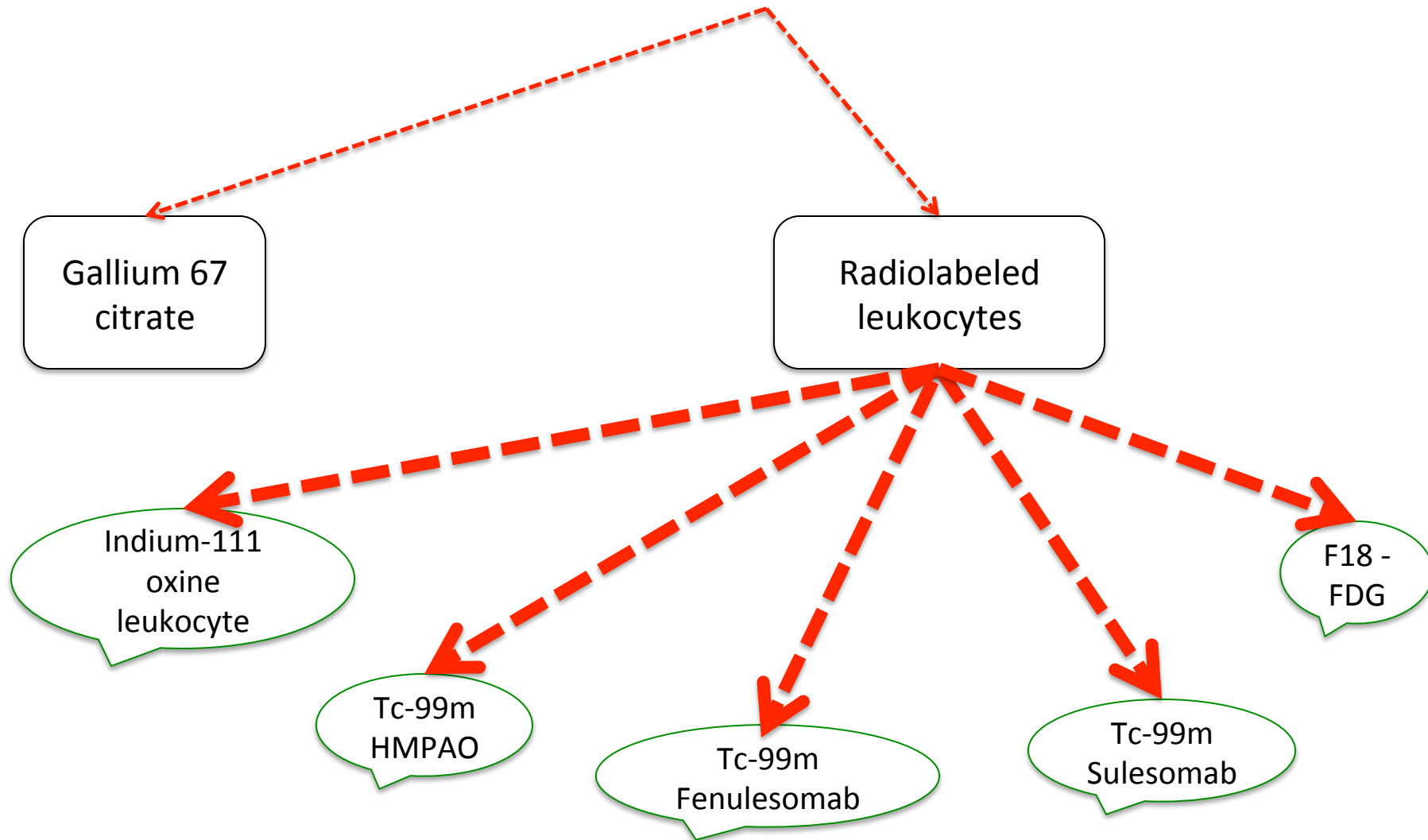
- Focal areas of uptake on Ga-67 scan are nonspecific and can represent either tumor or inflammation. Indium-111 leukocytes have been reported to localized in some neoplasms although this is uncommon occurrence.
- On Ga-67 imaging, sarcoidosis and lymphoma may have similar appearance. Both may show mediastinal and lymph node involvement. Sarcoidosis is suggested by the presence of the lambda sign and the panda sign. Abdominal involvement is more common in lymphoma.

Pearls & Pitfalls

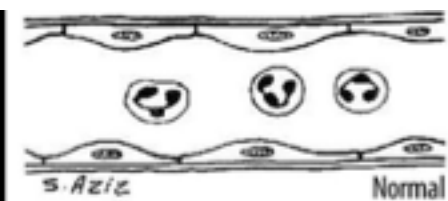
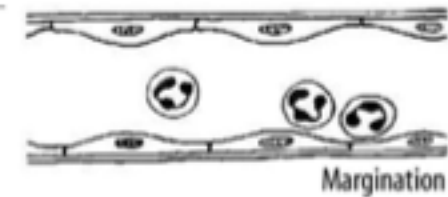
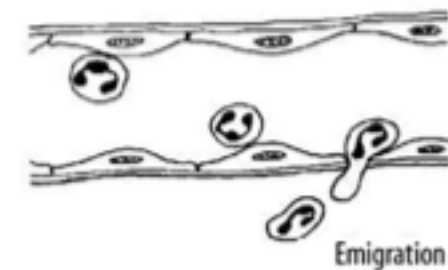
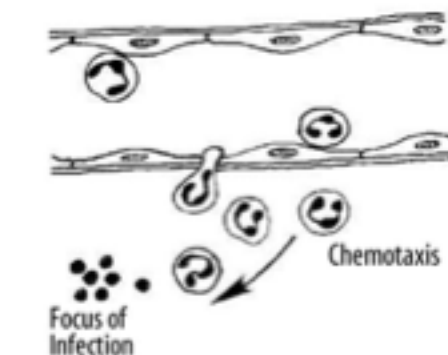
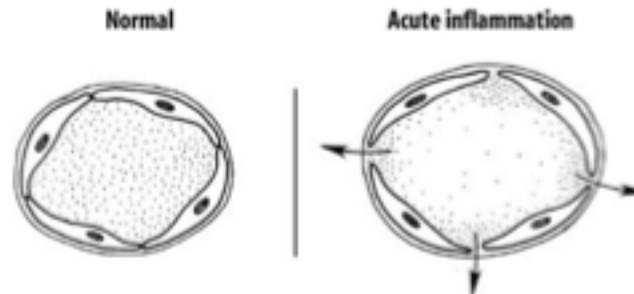
Infection and inflammation

- Diffuse lung uptake on Ga-67 scan is often due to PCP in patients with AIDS.
- Focal uptake in the abdomen on leukocyte scan may be due to an abscess or inflammatory bowel disease (Crohn's disease). Activity in the colon can be seen in ulcerative colitis or CMV.
- Ga-67 is preferred to labeled leukocyte in the setting of suspected spinal osteomyelitis.

Infection & inflammation



Pathophysiology of inflammation



Tissue injury/ infection
triggers inflammatory
reaction



Increased local blood flow
Increased vascular permeability



Emigration of leukocytes
out of blood vessels into
the tissues (chemotaxis)



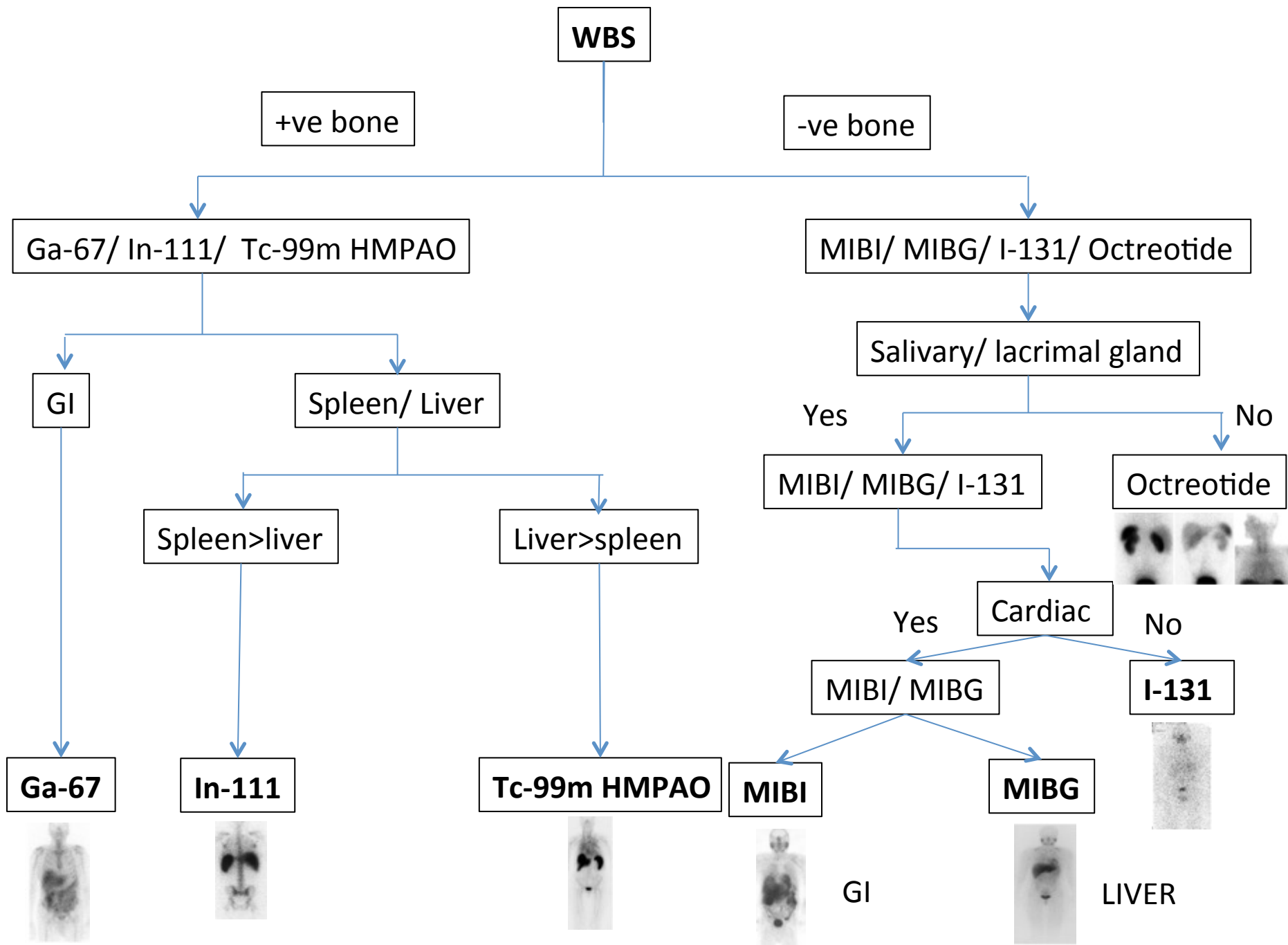
Polymorphonuclear
leukocytes and
macrophages ingest the
debris and foreign particles

Mechanisms

Mechanism	Radiopharmaceutical
Increased vascular permeability	^{67}Ga -citrate
Migration of WBCs to the site of infection	^{111}In - oxine or $^{99\text{m}}\text{Tc}$ -HMPAO -labelled autologous leukocytes $^{99\text{m}}\text{Tc}$ -Besilesomab
Binding to proteins at site of infection	^{67}Ga -citrate (lactoferrin and other iron containing proteins)
Binding to WBCs at site of infection	Chemotactic peptide Interleukin
Binding to bacteria	^{67}Ga -citrate $^{99\text{m}}\text{Tc}$ Infecton
Metabolic trapping	^{18}F -FDG

Radiopharmaceutical	Gallium-67 citrate	Indium-111 oxine leukocytes	Tc-99m HMPAO labeled leukocytes
Production of radionuclide	Cyclotron	Cyclotron	Generator
Decay mode	Electron capture	Electron capture	Isomeric transition
Half life	78hours	67hours	6hours
Photo peak (KeV)	93, 185, 288, 394	173, 247	140
Dose	5 mCi	0.3 – 0.5 mCi	5 – 10 mCi
Imaging time	48 hours	24 hours	1 - 4 hours
Normal biodistribution	Liver > indium, spleen, marrow, bone, gastrointestinal	Liver, spleen > Ga 67, marrow, lung	Liver, spleen, marrow, GI, GU and lung

Radiopharmaceutical	Gallium-67	Indium-111	Thalium-201
Half life	78 hours	67 hours	72 hours
Photo peak (KeV)	93, 185, 288, 394	173, 247	69-83, 135, 167



Normal Gallium-67 citrate Scan



Anterior



Posterior

- liver/spleen/GI
- marrow

Liver
Spleen
Marrow
Bone
Gastrointestinal

Normal biodistribution of ^{111}In -oxine labelled autologous leukocytes



Anterior



Posterior

***spleen intense than
liver/ marrow**

**Liver
Spleen
Marrow
Lung**

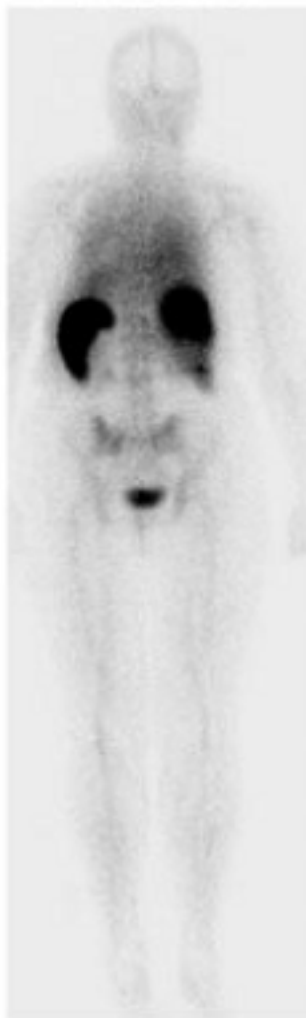
Normal biodistribution of ^{99m}Tc -HMPAO labelled autologous leukocytes

Anterior

Posterior

Anterior

Posterior



4 h



24 h

- liver/spleen/ bladder
- marrow

At 4hr, there is persistent blood-pool activity, activity is also seen in liver, spleen and GIT. (lungs)
At 24hr, blood-pool activity has cleared. Activity is present in bladder and colon, in addition to liver, spleen and bone marrow

Gallium-67 citrate imaging protocol

Patient preparation	No recent barium contrast study
Radiopharmaceutical	-Gallium-67 citrate -5 mCi -IV
Instrumentation	Photopeak :20% window, 93, 285 and 300 KeV Collimator: medium energy
Imaging procedure	24 hr images (optional):site of suspected infection if early intervention considered. 48 hrs images : whole body imaging Delayed 72 – 96 hr images : differentiate intraabdominal infection or normal bowel clearance

Indium-111 oxine leukocyte protocol

Patient preparation	Draw 50 ml of blood, radiolabel in vitro
Radiopharmaceutical	In-111 oxine labeled leukocyte 500 μ Ci
Instrumentation	Photopeak :20% window, 173 and 247 KeV Collimator: medium energy
Imaging procedure	4 hr images (optional):site of suspected acute abscess. 24 hrs images : whole body imaging

Tc-99m HMPAO leukocyte protocol

Patient preparation	Wound dressing should be changed prior imaging Draw 50 ml blood and radiolabeled in vitro
Radiopharmaceutical	Tc-99m HMPAO labeled leukocyte in vitro 10 mCi Given IV
Instrumentation	Photopeak :20% window, 140 KeV Collimator: low energy GP
Imaging procedure	1 - 2 hr images (mandatory):intra abdominal imaging 4 hrs images : peripheral skeletal imaging: osteomyelitis of feet Whole body imaging

Indications

Gallium-67	In-111 oxine leukocytes	Tc-99m HMPAO leukocytes
Severe leucopenia	Intra abdominal infection	Pediatric patients
Sarcoidosis	Cardiovascular infection	Inflammatory bowel disease
Idiopathic pulmonary fibrosis	Diabetic mid foot and hind foot osteomyelitis	Osteomyelitis of extremities including feet in non diabetic
Pulmonary drug reactions (amiodarone, bleomycin)	Inflammatory bowel disease	Diabetic forefoot osteomyelitis
Pneumocystic carinii	Hip and knee prosthesis	
FUO	Orthopedic hardware, prior fracture or infection	
Immunosuppressed patient with lung infections		
Suspected low grade chronic infections (fungal/protozoa)		

	¹¹¹ In- oxine labelled leukocytes	^{99m} Tc-HMPAO- labelled leukocytes
Advantages	<ol style="list-style-type: none"> 1. Stable label 2. Constant biodistribution limited to liver, spleen, bone marrow 3. Physical half life of 67hr allows for delayed imaging which is valuable for musculoskeletal infection 4. In musculoskeletal inf, bone or marrow scintigraphy can be performed simultaneously as dual-isotope acquisition, or immediately after this study 	<ol style="list-style-type: none"> 1. Photon energy that is optimal for imaging 2. High photon flux as more radioactivity is injected 3. Ability to detect abnormalities within a few hours after injection

	¹¹¹ In- oxine labelled leukocytes	^{99m} Tc-HMPAO- labelled leukocytes
Disadvantages	<ol style="list-style-type: none"> 1. Low photon flux 2. Less than ideal photon energy 3. Imaging done 24 hours after injection 	<ol style="list-style-type: none"> 1. Genitourinary tract activity appear shortly after injection, colonic activity appear by 4 hrs after injection 2. Not useful to detect infection that tend to be indolent, for which several hours maybe necessary for accumulation of sufficient labelled leukocytes to be successfully imaged

^{99m}Tc -diphosphonates (triple phase bone scan)

- 3 phase bone scan:
 - FLOW PHASE
 - BLOOD POOL AND SOFT TISSUE PHASE
 - SKELETAL PHASE (DELAYED IMAGES)

- Important to differentiate **osteomyelitis** from **cellulitis** because therapy for osteomyelitis requires prolonged therapy

Scintigraphic finding of osteomyelitis

- Early or arterial hyperaemia
- Focally and possibly diffusely increased radiotracer uptake on blood pool images
- Progressive focal accumulation in the involved bone on delayed images (with relative soft tissue clearance)

Scintigraphic finding of cellulitis

- Delayed or venous phase hyperaemia
- Increased blood pool images activity
- No focally increased uptake in bone on delayed images (with persistent soft tissue activity)

Osteomyelitis

- Nuclear medicine studies used in workup of osteomyelitis include triple phase bone scan, ^{67}Ga and labeled leukocyte scintigraphy.
- Triple phase bone scan is the study of choice in diagnosing osteomyelitis in bones not affected by underlying conditions.
- Bone scan abnormalities reflect the rate of new bone formation in general, consequently, fractures, orthopedic hardware, or neuropathic joint can yield positive scan. In these situations, bone scan because of its decreased specificity, is less useful.
- Specificity can be improved by addition of ^{67}Ga scintigraphy.

- Combined bone/ ^{67}Ga imaging is:
- ✓ Positive for osteomyelitis when distribution of the 2 tracers is spatially incongruent or when the distribution is spatially congruent but the relative intensity of uptake of ^{67}Ga is greater than that of the bone agent
- ✓ Negative when ^{67}Ga images are normal, regardless of bone scan finding, or when the distribution of the 2 tracers is spatially congruent but the relative intensity of uptake of ^{67}Ga is less than that of the bone agent.
- ✓ Equivocal when distribution of 2 tracers is congruent, both spatially and in intensity
- Overall accuracy of bone/ ^{67}Ga imaging is 65 – 80% (Palestro et al radionuclide imaging in orthopedic infections)

Osteomyelitis in different clinical situations

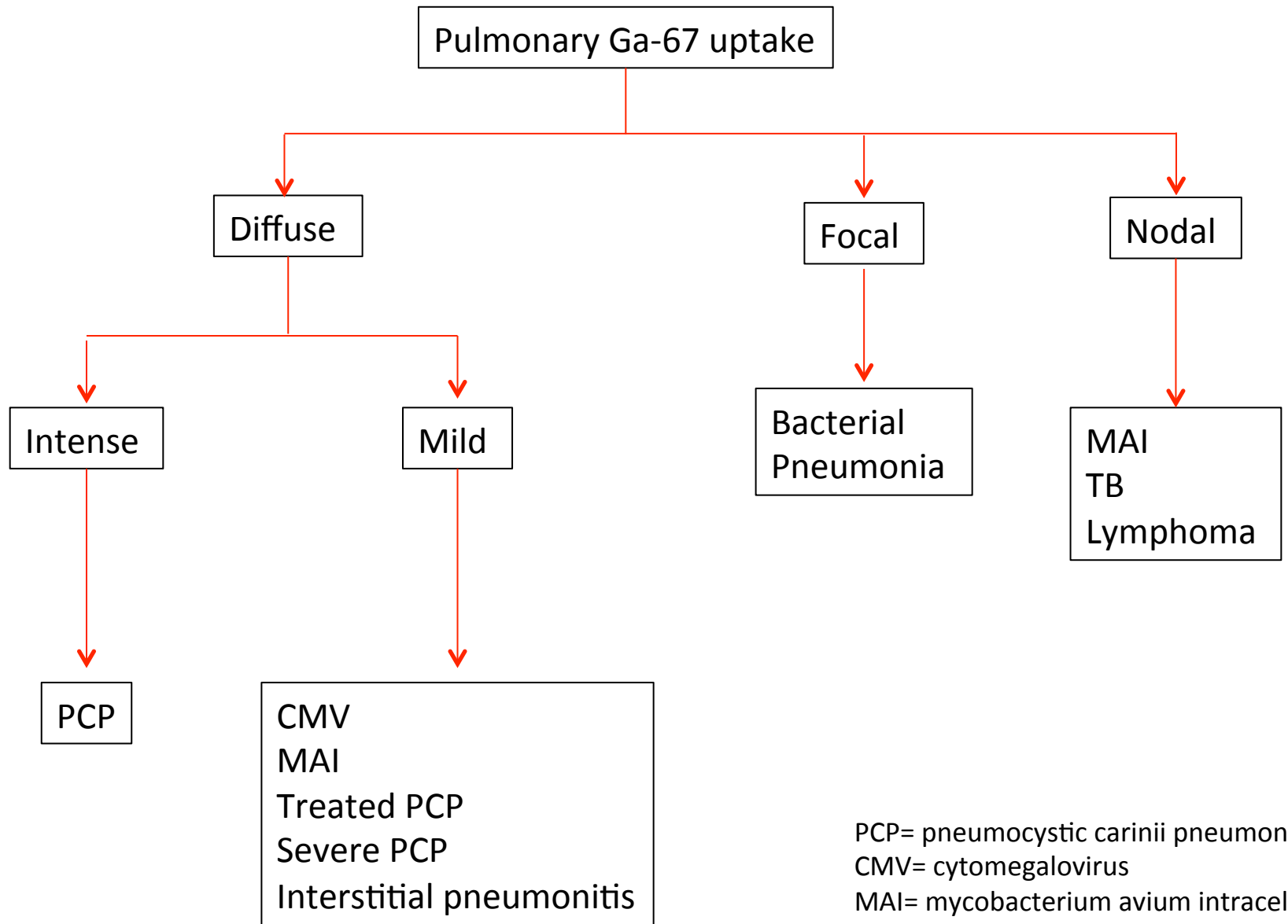
Normal x ray	Three phase Bone scan
Neonates	Three phase bone scan and if negative for Tc-99m HMPAO
Suspected osteomyelitis in non marrow skeleton (distal extremities)	Bone scan + leukocyte scan
Suspected osteomyelitis in bone marrow containing skeleton (knees and hips)	Marrow scan + leukocyte scan
Vertebral osteomyelitis	Ga - 67

Osteomyelitis

Type of study	Sensitivity %	Specificity %
Three phase bone scan (normal x ray)	94	95
Three phase bone scan (underlying disease)	95	33
Gallium 67	81	69
Indium-111 oxine leukocytes	88	85
Tc-99m HMPAO leukocytes	87	81
MRI	95	87

Infections

Regions	Scans
Diabetic foot	Distal foot – Tc-99m HMPAO leukocytes Mid/hind foot – In-111 leukocytes
Vertebral osteomyelitis	Ga-67/bone scan F18-FDG Tc-99m infecton
Infected joint prosthesis	In-111 leukocytes/ Tc-99m SC accuracy 90%
Intra abdominal infections	In-111 leukocytes sensitivity 90% @ 24 Hr imaging Tc-99m HMPAO leukocytes @ 2 Hr imaging Tc-99m Fanolesomab for acute appendicitis
Inflammatory bowel disease	Tc-99m HMPAO : Crohn's small bowel involvement Ulcerative colitis = colonic involvement without small bowel
Cardiovascular	Prosthetic graft – In-111 leukocytes d/t no blood pool
Renal	Ga-67 * increased uptake may due to renal/hepatic failure and iron overload
Intra cerebral	Tl-201 : increased uptake = malignant, no uptake = infection
FUO	Ga-67 Post op fever=In-111 leukocytes
Malignant external otitis	Ga-67



PCP= pneumocystic carinii pneumonia
CMV= cytomegalovirus
MAI= mycobacterium avium intracellular

Gallium-67	Thallium-201	
- ve	+ ve	Kaposi's sarcoma
+ ve	- ve	Infection
+ ve	+ ve	Lymphoma

**Abnormal CXR
& Normal
Gallium-67**

Kaposi's sarcoma

Pulmonary fibrosis

**Treated
sarcoidosis**

Inactive TB

Normal CXR & Abnormal Gallium-67	PCP
	CMV
	Sarcoidosis
	Pulmonary drug toxicity
	Lymphocytis interstitial pneumonitis

Gallium scan 100% sensitivity	Burkitt's lymphoma
	Pyogenic acute osteomyelitis
	Pyogenic acute arthritis

Gallium-67 lung uptake associated with drugs	Bleomycin
	Amiodarone
	Busulfan
	Nitrofurantoin
	Cyclophosphamide
	Methotrexate

Ga-67 is taken up by the lungs due to drug toxicity. Which drugs are the culprits?

Ga-67 is taken up by the lungs due to drug toxicity. Which drugs are the culprits?

- Bleomycin is the most common. Uptake can be seen with cytoxin, nitrofurontoin and amiodarone.

What is the role of Ga-67 in sarcoidosis?

What is the role of Ga-67 in sarcoidosis?

- Ga-67 lung uptake is a sensitive test for the diagnosis of active alveolitis of sarcoidosis. Ga-67 may be markedly increased in the setting of a normal CXR in early disease and may be negative in the setting of an abnormal CXR in inactive disease.

Which leukocytes are labeled with
In-111 oxine and Tc-99m HMPAO?

Which leukocytes are labeled with In-111 oxine and Tc-99m HMPAO?

- In-111 binds to neutrophils, lymphocytes, monocytes, erythrocytes and platelets.
- Tc-99m HMPAO binds to neutrophils.

Which of the following statements is true regarding In-111 oxine leukocytes?

- A. It is diagnostically useful for evaluating inflammatory lung disease.
- B. It has a high sensitivity for detecting osteomyelitis in the spine.
- C. It should be used when the peripheral leukocyte count is less than $3000/\text{mm}^3$.
- D. It is the radiopharmaceutical of choice for intraabdominal infection.

Which of the following statements is true regarding In-111 oxine leukocytes?

- FFTT

What is the optimal imaging time for
In-111 leukocytes and Tc-99m HMPAO
leukocytes?

What is the optimal imaging time for In-111 leukocytes and Tc-99m HMPAO leukocytes?

- In-111 labeled leukocytes are routinely imaged at 24 hours. Imaging at 4 – 6 hours is less sensitive for detection of infection. The one exception is inflammatory bowel disease in which imaging should be done at 4 hours because intraluminal shedding of inflamed cells may result in inaccurate localization at 24 hours.
- Tc-99m HMPAO leukocytes should be imaged at 1 -2 hours for intraabdominal infection because of biliary and renal clearance seen by 2 hours. Extra abdominal infection can be imaged later, usually 4 hours allowing more time for background clearance.

Regarding osteomyelitis, which of these statements are true?

- A. The three phase bone scan is sensitive test for diagnosis.
- B. The three phase positive scan is specific for osteomyelitis.
- C. A negative flow phase study almost always rules it out.
- D. In patients with prostheses, a bone marrow scan can be useful to rule out a false positive In-111 leukocyte study.

Regarding osteomyelitis, which of these statements are true?

- TTTF

Which of the following statement are true?

- A. A negative three phase bone scan exclude osteomyelitis with high degree of certainty.
- B. The specificity of bone scan is poor in patients with underlying bone disease such as fractures, orthopedic hardware and neuropathic joints.
- C. In-111 oxine and Tc-99m HMPAO leukocytes have poor specificity for the diagnosis of osteomyelitis in a patient with a hip prosthesis.
- D. Because the three phase bone scan may be positive in a patient with a Charcot's joint, a radiolabeled leukocyte study should be performed.

Which of the following statement are true?

A. TTTF

In the imaging of the lung infection

- A. Gallium uptake is highly sensitive for PCP
- B. Localized uptake of Gallium is common in PCP
- C. Uptake of Indium-111 labeled white cells in the lungs is relatively non specific for infection
- D. Unmatched defects of perfusion are the most common abnormality seen on V/Q scan in patients with bacterial infection
- E. In patients with TB, only sites of active infection are Gallium avid

In the imaging of the lung infection

- TFTFT

Concerning In-111 white cell scans

- A. The white cells must be autologous
- B. Lung activity is pathological between 1 and 4 hours after injection
- C. If a focus of increased uptake is seen on the early images, the 24 hour images do not need to be performed
- D. In-111 white cell are more useful in chronic PUO
- E. If the patient is on appropriate antibiotics, the white cell study is unlikely to be positive

Concerning In-111 white cell scans

- FTFFF

Concerning Tc-99m HMPAO and In-111 labeled white cell scans

- A. Diffuse bowel activity on a Tc-99m HMPAO study at 24 hrs indicates severe colitis
- B. On a Tc-99m HMPAO labeled white scan, the typical appearances of IBD is intense activity at 1 hour which fades with time
- C. Rectal disease can be distinguished from bladder activity on a Tc-99m HMPAO
- D. Activity is seen in the bowel in IBD because the labeled WBC's fix in the inflammatory bowel wall
- E. An abscess that communicates with the bowel can be distinguish from one that does not

Concerning Tc-99m HMPAO and In-111 labeled white cell scans

- FFTFT

Concerning the imaging of the immunosuppressed patient

- A. In-111 labeled WBCs are sensitive as Gallium at detecting PCP
- B. Tc-99m DTPA clearance is more useful than Gallium scanning in the following up of PCP
- C. Gallium uptake in the colon is highly suspicious for acute colitis
- D. Kaposi's lesions take up Tl-201
- E. Active MAI infection in HIV positive patients has specific appearance on Gallium scan

Concerning the imaging of the immunosuppressed patient

- FTFTF

The source of lectoferrin

- A. Lymphocytes
- B. Leucocytes
- C. Bacteria
- D. Fungus
- E. Tissue macrophage

The source of lectoferrin

- FTFFF

The source of siderophores

- A. Lymphocytes
- B. Leucocytes
- C. Bacteria
- D. Fungus
- E. Tissue macrophage

The source of siderophores

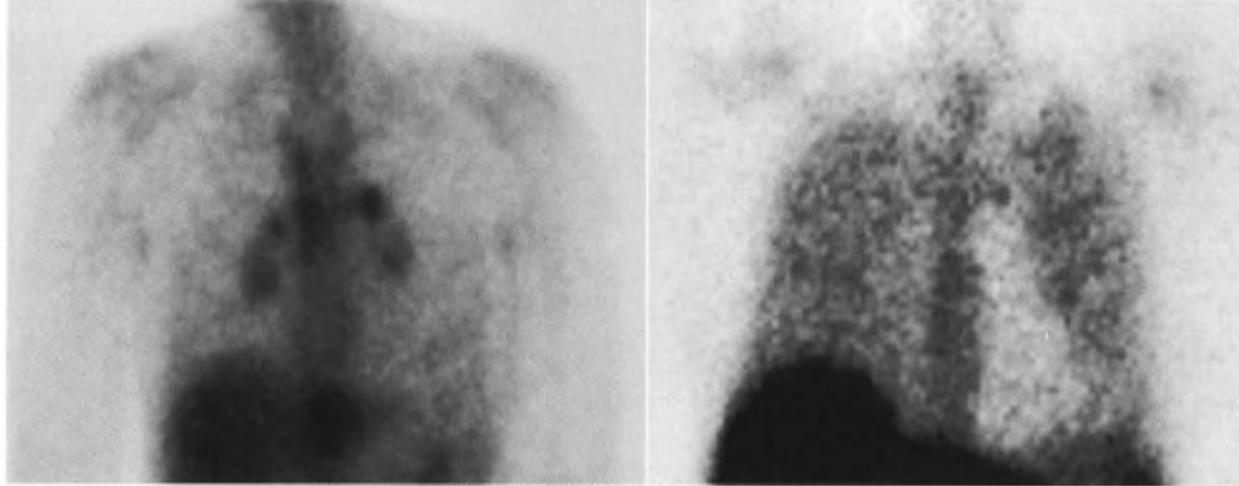
- FFTFF

Lactoferrin is physiologically produced by certain organs that localize gallium

- A. Lacrimal glands
- B. Salivary glands
- C. Lactating breast
- D. Bone
- E. Liver

Lactoferrin is physiologically produced by certain organs that localize gallium

- TTTF



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A



B

Two patients with the same disease (*A* and *B*) had ^{67}Ga scintigraphy.

1. Describe the lung patterns seen on the ^{67}Ga lung scans.
2. What is the finding on the head and neck scan?
3. Match the lung scan with the head and neck scan.
4. What is the disease, and how is ^{67}Ga scintigraphy used in these patients?

Sarcoidosis

1. Patient A: lambda sign (hilar and paratracheal nodal uptake). patient B: diffuse pulmonary uptake.
2. Classic panda sign.
3. Either A or B. The panda sign can be seen at any stage of the disease.
4. Sarcoidosis. Ga-67 scan is used to confirm the clinical diagnosis and differentiate active alveolitis from inactive fibrosis.

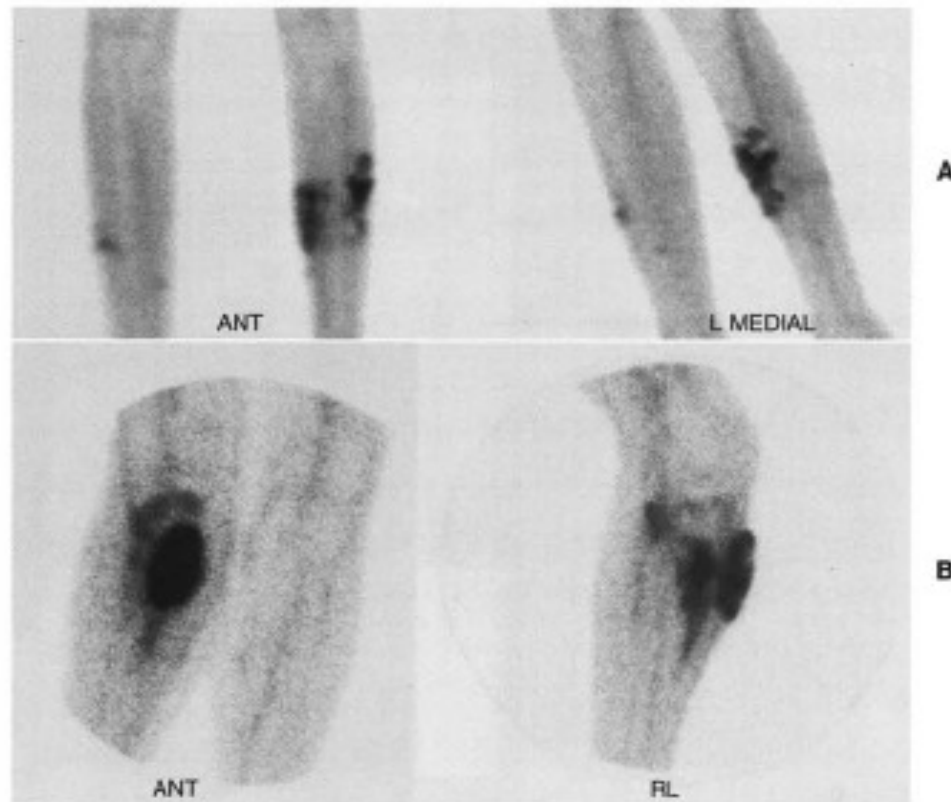


A 57-year-old man has had abdominal discomfort and fever for 3 weeks.

1. Describe the findings on this ^{67}Ga study and give a likely diagnosis.
2. What is the mechanism of ^{67}Ga uptake in infection/inflammation?
3. List the photopeaks of ^{67}Ga . List the ones used for imaging. What collimator should be used to acquire the study?
4. What is the recommended administered dose of ^{67}Ga , its half-life, and imaging times?

Intraabdominal abscess

1. Very increased uptake in the right lower quadrant strongly suggests an intraabdominal abscess. Tumor cannot be excluded.
2. Increased vascular permeability, bacterial uptake and binding to leukocytes play a role, however, binding to lactoferrin of degranulated neutrophils at the site of infection is probably the primary mechanism.
3. Photopeak at 91 to 93, 185, 300 and 394 keV. The lower three photopeaks are used for imaging. A medium energy collimator should be used.
4. The recommended adult dose of Ga-67 is 5 mCi, half life is 78 hours, imaging time is at 48 hours is routine. If abscess suspected, imaging at 6 to 24 hours may provide an early diagnosis.



Two patients (*A* and *B*) with similar histories of a soft tissue infection overlying the tibia. ^{99m}Tc HM-PAO leukocyte studies were ordered to confirm or exclude underlying osteomyelitis.

1. Would a bone scan be useful as the initial study in these cases?
2. When would a bone marrow study with ^{99m}Tc sulfur colloid be useful in this clinical setting?
3. Would an ^{111}In oxine leukocyte study or ^{67}Ga study be preferable?
4. Describe the findings. What are the diagnoses?