



DNB EXIT EXAMINATION • NUCLEAR MEDICINE

DNB Nuclear Medicine

Solved Previous-Year Questions

Exit examination • June 2020 – December 2025 • Papers I–IV

VOLUME 1

Basic Sciences: Physics, Instrumentation,
Radiopharmacy, Radiobiology & Safety,
Biostatistics

12

SESSIONS

135

SOLVED ANSWERS

6

YEARS

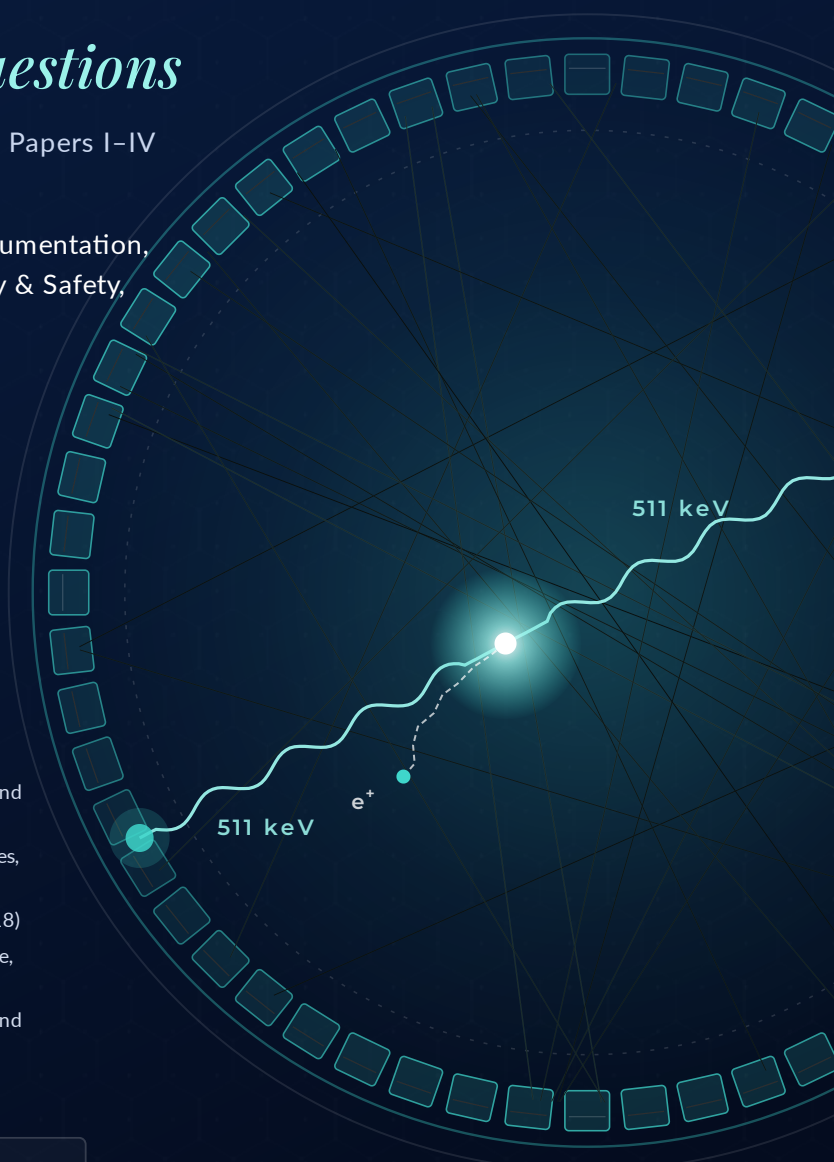
SOURCES • ANSWERS REFERENCED TO

MET 7e	Mettler & Guiberteau, Essentials of Nuclear Medicine and Molecular Imaging, 7th ed (2019)
REQ 5e	Nuclear Medicine and Molecular Imaging: The Requisites, 5th ed (2021)
SAHA 7e	Saha, Fundamentals of Nuclear Pharmacy, 7th ed (2018)
CSP 4e	Cherry, Sorenson & Phelps, Physics in Nuclear Medicine, 4th ed (2012)
IAEA 2014	Nuclear Medicine Physics: A Handbook for Teachers and Students

REVIEWED BY

Dr Gaurav Sharma & Dr Aditi Pal

DNB Nuclear Medicine





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MEDICAL EXAM SERIES

DNB EXIT EXAMINATION

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Basic Sciences: Physics, Instrumentation, Radiopharmacy, Radiobiology & Safety, Biostatistics

June 2020 – December 2025 • 12 sessions • Papers I–IV

Updated till October 2026

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How to use these notes

- **One answer, many questions.** Repeated and near-repeated questions are answered once. Each answer heading lists every version with its paper tag; the badge (1×, 2×, 3×, 4×+) shows how often it was asked.
- **Red box: NOT COVERED IN SOURCE.** The point was searched in all five textbooks (full text and index) and is not there. The box names the searches.
- **Amber box: current guideline.** An official guideline or consensus document (body, document, year), placed after the main answer.
- **Figures.** Book figures carry their own figure number and page. Schematics are original simplified exam diagrams and are labelled "Schematic (exam diagram)".
- **Sources.** MET 7e = Mettler & Guiberteau, Essentials of Nuclear Medicine and Molecular Imaging, 7th ed (2019); REQ 5e = Nuclear Medicine and Molecular Imaging: The Requisites, 5th ed (2021; e-book pages); SAHA 7e = Fundamentals of Nuclear Pharmacy, 7th ed (2018); CSP 4e = Physics in Nuclear Medicine, 4th ed (2012); IAEA 2014 = Nuclear Medicine Physics: A Handbook for Teachers and Students.

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PART 1

Basic Nuclear Physics

A1 Atomic & nuclear structure

[1×] A1-01 • 10 marks

Explain what is meant by binding energy of the nucleus. Explain the meaning of the terms: mass difference, columbic barrier and the relationship between the mass difference and binding energy of a nucleus. What should be the minimum energy of Cyclotron to produce F-18? [3+3+4]

Asked in: Dec 2021 Paper I Q1

Binding energy of the nucleus

- When the mass of an atom is compared with the sum of the masses of its protons, neutrons and electrons, it is always less by an amount Δm .

- This mass deficiency, expressed in energy units, is the **binding energy** E_B :

$$E_B = \Delta m \cdot c^2 \quad (1 \text{ u} = 931.5 \text{ MeV})$$

- E_B is the **minimum energy needed to separate the atom completely into its components**. Most of it is **nuclear binding energy** (separating the nucleons); the orbital-electron share is small.
- Equivalently, it is the energy **liberated when Z protons and (A – Z) neutrons come together** to form the nucleus.
- Binding energy per nucleon (E_B/A)** is of the order of **~8 MeV per nucleon**. It rises steeply at low A, peaks at about **8.7 MeV/nucleon near A ≈ 60** (Fe, Co, Ni: the most stable nuclei), and falls gently for heavy nuclei.
- The **larger E_B/A , the more stable** the nucleus. Removing a single nucleon needs about **6–9 MeV**.

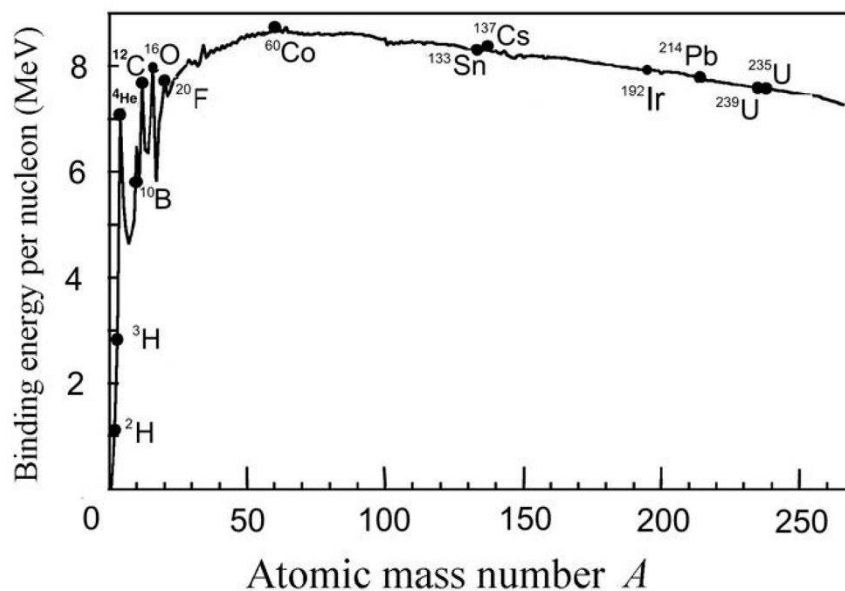


FIG. 1.1. Binding energy per nucleon in megaelectronvolts per nucleon against atomic mass number A. Data are from the National Institute of Science and Technology (NIST).

Fig. 1.1. IAEA 2014, p. 13.

Worked example — Binding energy of a C-12 atom (book values)

- Components: 6 electrons ($6 \times 0.000549 \text{ u}$) + 6 protons ($6 \times 1.007276 \text{ u}$) + 6 neutrons ($6 \times 1.008665 \text{ u}$) = **12.098940 u**.
- Mass of C-12 = 12 u (by definition) $\Delta m = \mathbf{0.098940 \text{ u}}$.
- $E_B = 0.098940 \times 931.5 \text{ MeV} = \mathbf{92.16 \text{ MeV}}$ ($\approx 7.68 \text{ MeV}$ per nucleon).

Mass difference (mass defect)

- **Mass defect (Δm)**: the mass of a nucleus is always less than the combined masses of its individual nucleons. This difference is the **mass defect** (deficit). It has been "used as energy" in binding the nucleons together.
- In any nuclear reaction, the difference between (target + projectile) masses and (product + emitted particle) masses gives the **Q-value**. It is positive for exothermic reactions (all spontaneous decays) and **negative** for most charged-particle production reactions, which therefore need energy input.

Relationship between mass difference and binding energy

- Binding energy is simply the **energy equivalent of the mass defect**, $E_B = \Delta m c^2$.
- Nuclear processes that **release energy always increase the binding energy** and reduce the mass. A nucleus that emits a 1-MeV γ ray weighs less, by the mass equivalent of 1 MeV, afterwards: **mass is converted to energy**.
- Example: a free proton and neutron fuse to deuterium. The 2.2-MeV mass difference is released as a γ photon, and at least 2.2 MeV must be supplied to split the deuteron.

Coulombic (Coulomb) barrier

- Protons repel each other through **long-range coulombic (electrical) forces**. These are countered by **very strong short-range attractive nuclear (exchange) forces** acting only between close neighbours.
- A **positively charged projectile** (proton, deuteron, α particle) approaching a nucleus is repelled by these coulombic forces. This repulsion is the **Coulomb barrier**.
- Charged particles must therefore be accelerated to **high energies, typically 10–20 MeV**, to penetrate the nucleus. **Neutrons**, being uncharged, can enter even at thermal energies (0.025 eV).
- Consequence: a **threshold** exists for charged-particle reactions that is absent for neutrons. The **threshold energy must exceed $|Q|$** , because the Coulomb energy has to be added to the Q-value.
- Example: $^{14}\text{N}(\text{p},\alpha)^{11}\text{C}$ needs at least **2.93 MeV** ($|Q|$), but its threshold is **3.14 MeV**.

Minimum cyclotron energy to produce F-18

- Reaction of choice: $^{18}\text{O}(\text{p},\text{n})^{18}\text{F}$, on enriched ^{18}O -water.
- **Threshold energy = 2.57 MeV** (≈ 2.5 MeV on the excitation function); below this **no F-18 can be produced**.
- The activation cross-section is a **strong function of proton energy** (Fig. 5-8); charged particles for production are typically accelerated to **10–20 MeV**.
- The proton energy needed is **low**, so a **low-cost accelerator** suffices. This, plus high yield, makes $^{18}\text{O}(\text{p},\text{n})$ the reaction of choice despite the expensive enriched target.
- Alternative: $^{20}\text{Ne}(\text{d},\alpha)^{18}\text{F}$ (threshold 0 MeV) is difficult because F-18 sticks to target walls. $^{16}\text{O}(\alpha,\text{d})^{18}\text{F}$ needs 35-MeV α particles (expensive accelerators).

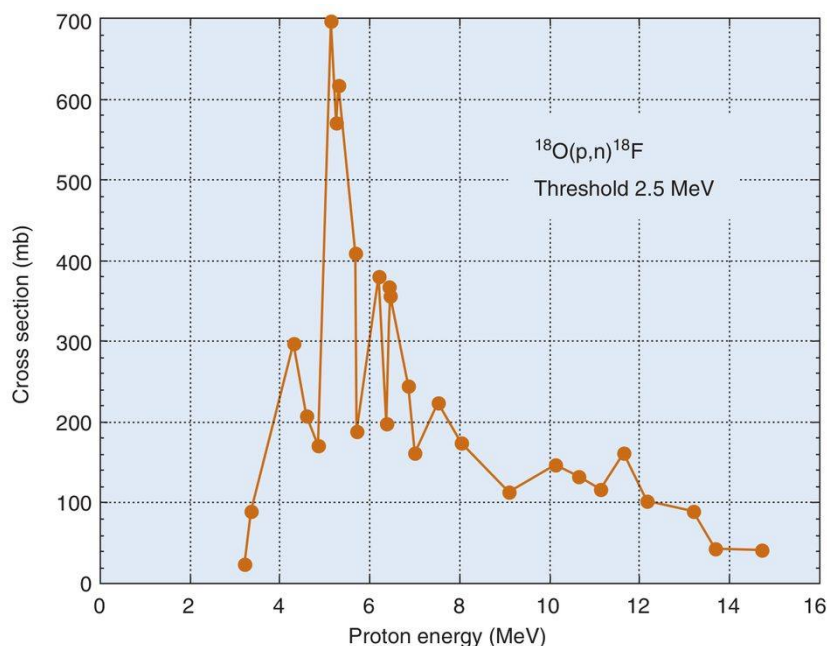


FIGURE 5-8 Activation cross-section versus particle energy for the reaction $^{18}\text{O}(p,n)^{18}\text{F}$. The energy threshold for this reaction is ~2.5 MeV. [From Ruth TJ, Wolf AP: *Absolute cross sections for the production of ^{18}F via the $^{18}\text{O}(p,n)^{18}\text{F}$ reaction*. Radiochim Acta 26:21-24, 1979.]

Figure 5-8. CSP 4e, p. 54.

Table A1-01.1. Thresholds of some cyclotron reactions (CSP Table 5-2)

Product	Reaction	Threshold (MeV)
F-18	$^{18}\text{O}(p,n)^{18}\text{F}$	2.57
F-18	$^{20}\text{Ne}(d,\alpha)^{18}\text{F}$	0
C-11	$^{14}\text{N}(p,\alpha)^{11}\text{C}$	3.1
N-13	$^{16}\text{O}(p,\alpha)^{13}\text{N}$	5.5
Ga-67	$^{68}\text{Zn}(p,2n)^{67}\text{Ga}$	5.96

Pearls

- $E_B = \Delta m c^2$; 1 u = 931.5 MeV; C-12 binding energy 92.16 MeV.
- $E_B/A \approx 8$ MeV, peaking at **8.7 MeV near $A \approx 60$** : the most stable nuclei.
- Charged particles need **10–20 MeV** to overcome the Coulomb barrier; neutrons need none.
- **F-18 threshold 2.57 MeV** for $^{18}\text{O}(p,n)$; threshold $> |Q|$ because of the Coulomb barrier.

Sources

- CSP 4e, ch. 2 "Basic Atomic and Nuclear Physics", §D.4 "Forces and Energy Levels within the Nucleus", §D.6 "Nuclear Binding Energy" and §D.7, pp. 14–16, Eq. 2-5, Table 2-2 p. 13.
- CSP 4e, ch. 5 "Radionuclide and Radiopharmaceutical Production", §B.1 "Charged-Particle Accelerators", p. 47; Table 5-2, p. 50; §D.1–2 "Activation Cross-Sections", p. 54; Fig. 5-8, p. 54.
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.3.2 "Nuclear binding energy", p. 12, Fig. 1.1, p. 13 (second book: binding energy per nucleon curve).
- IAEA 2014, ch. 4 "Radionuclide Production", §4.1.3 "Binding energy, Q-value, reaction threshold", pp. 123–124; §4.1.4, p. 125; §4.2, p. 128; Table 4.3, p. 138 (second book: Q-value, threshold $> Q$, reactions for F-18).
- SAHA 7e, ch. 1 "The Atom", §1.3, p. 8; ch. 4 "Production of Radionuclides", §4.1, pp. 50–51 (second book: mass defect wording, Coulomb energy added to Q).

Niel Bohr's atomic model with diagram. [5]

Asked in: Jun 2023 Paper I Q5b

Background

- **Rutherford (1910):** the atom has a **massive, compact, positively charged nucleus** surrounded by a diffuse cloud of light, negative electrons. By classical theory, orbiting electrons should lose energy and **spiral into the nucleus** ("atomic collapse"), which does not happen.
- **Niels Bohr (1913)** refined this model using postulates that combine classical mechanics with **quantisation of angular momentum**.

Postulates / main features of the Bohr atom

- Electrons revolve around the nucleus in a set of **stable orbits (shells)** in which they can exist **indefinitely without loss of energy**.
- Shell diameters are fixed by the **principal quantum number n** (integers 1, 2, 3 ...): **K ($n = 1$), L ($n = 2$), M ($n = 3$), N ($n = 4$)**.
- Angular momenta, orbit radii, electron velocities and binding energies are all **quantised**: only discrete values are allowed.
- **Energy is emitted or absorbed only when an electron moves between shells**. Moving to an outer shell needs energy equal to the difference in binding energies; dropping to an inner shell **releases a photon** of exactly that energy (characteristic radiation).
- **Binding energy** is greatest for the innermost shell ($K_B > L_B > M_B$) and increases with Z .

Refinements (Pauli principle, quantum numbers)

- Each shell has **$2n - 1$ substates** (K: 1; L: L_I, L_{II}, L_{III}).
- **Pauli exclusion principle (1925)**: no two electrons can have exactly the same motion, so a shell holds at most **$2n^2$ electrons**: K 2, L 8, M 18, N 32.
- Further quantum numbers: azimuthal ($l = 0 \dots n - 1$; s, p, d, f orbitals), magnetic (m) and spin ($s = \pm\frac{1}{2}$).

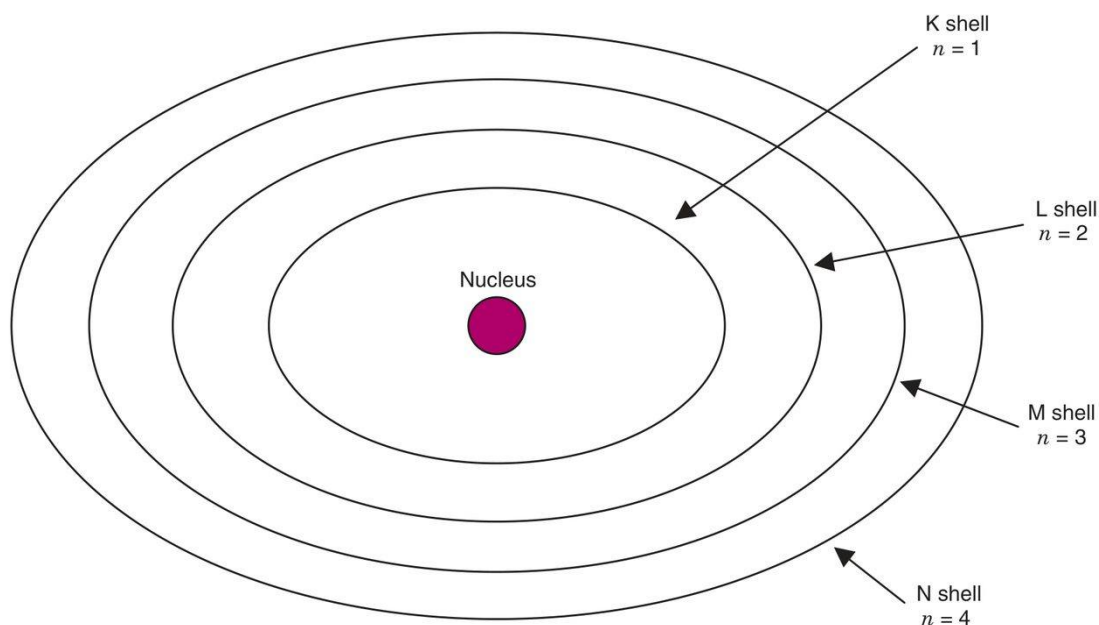
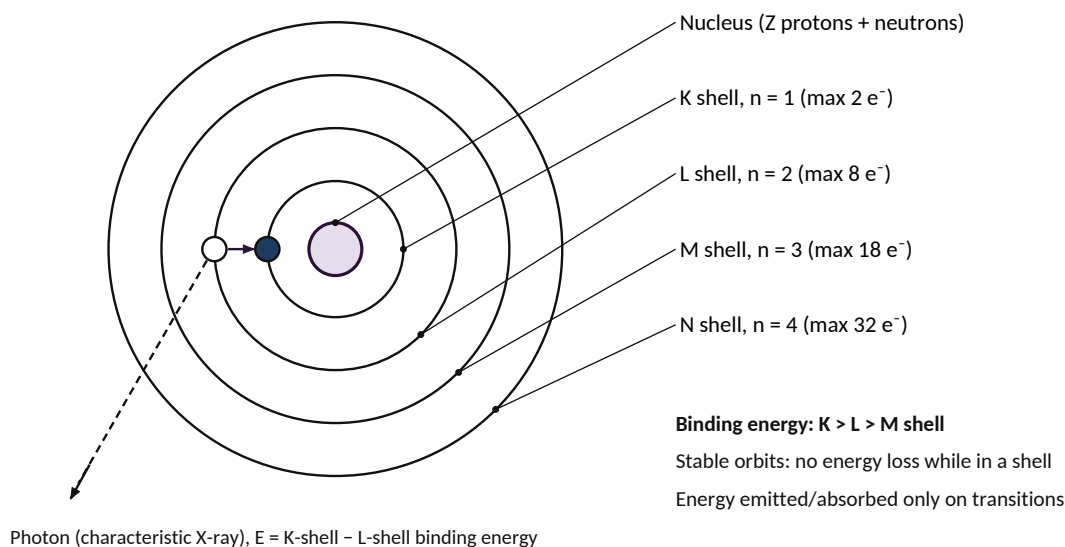


FIGURE 2-2 Schematic representation of the Bohr model of the atom; n is the quantum number of the shell. Each shell has multiple substates, as described in the text.

Figure 2-2. CSP 4e, p. 10.



Schematic (exam diagram): Bohr model of the atom with shells and an L→K transition. Based on CSP 4e, Fig. 2-2, p. 10 and Fig. 2-4, p. 11; text pp. 9-11; SAHA 7e, pp. 1-2.

Limitations

- An **oversimplification**: electrons do not move in precise circular orbits but in imprecisely defined regions of space, sometimes even passing through the nucleus.
- It successfully handles **one-electron systems** (H, He⁺, Li²⁺). It is still adequate for nuclear-medicine purposes and for teaching.

Relevance to nuclear medicine

- Explains **characteristic X-rays and Auger electrons** (inner-shell vacancy filling) after electron capture and internal conversion.
- Explains why a photoelectron cannot be ejected from a shell unless the photon energy **exceeds that shell's binding energy**.

Pearls

- Shells K, L, M, N = n 1, 2, 3, 4; maximum electrons **2n²**.
- **K_B > L_B > M_B**; binding energy rises with Z (iodine K-shell 33.2 keV).
- Photon energy on transition = **difference in binding energies** of the two shells.

Sources

- CSP 4e, ch. 2 "Basic Atomic and Nuclear Physics", §C.1 "Composition and Structure" and §C.2 "Electron Binding Energies and Energy Levels", pp. 9-11; Fig. 2-2, p. 10; Fig. 2-4, p. 11.
- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §C.1 (photoelectric effect and shell binding energy), p. 74.
- SAHA 7e, ch. 1 "The Atom", §1.1 "Electronic Structure of the Atom", pp. 1-2, Table 1.1 (second book: quantum numbers l, m, s and 2n² per shell).
- IAEA 2014, ch. 1, §1.2.1 "Rutherford model" and §1.2.2 "Bohr model of the hydrogen atom", p. 10 (second book: quantisation postulates and one-electron limitation).

[3×] A2-01 • 5 marks

Auger electrons & characteristic X-rays

- › Define following: Auger Electron — Jun 2020 • Paper I • Q9a
- › Characteristic X-rays and Auger electrons. [5] — Jun 2023 • Paper I • Q6a
- › Auger electron. [5] — Dec 2023 • Paper I • Q6a

Asked in: Jun 2020 Paper I Q9a • Jun 2023 Paper I Q6a • Dec 2023 Paper I Q6a

How an inner-shell vacancy arises

- An electron removed from an inner shell (K, L) leaves a **vacancy**. Causes: energy delivered by a **particle or photon striking the atom**, and the vacancies left by **electron capture** and **internal conversion**.
- An electron from an outer shell promptly fills the vacancy. The energy released equals **exactly the difference in binding energies** of the two shells. It leaves the atom in one of two ways.

Characteristic X-rays

- The released energy appears as a **photon**. Binding-energy differences have **exact, characteristic values for each element**, hence "**characteristic radiation / X-rays**".
- **Notation:** K_{α} (vacancy in K filled from L: $K\alpha_1$ from L_{III} , $K\alpha_2$ from L_{II}); K_{β} (filled from M or N); L_{α} , L_{β} for L-shell vacancies. Some transitions are forbidden by quantum selection rules ($K \leftarrow L_I$).
- Energy is **discrete (line spectrum)**. A K X-ray's energy is always **less than the K-shell binding energy**, so it cannot eject a K electron of the same atom.
- Example: **Tl-201 (EC)** emits **69–83 keV X-rays** of its daughter (93% abundance). EC daughters with $Z \geq 50$ emit K X-rays >25 keV, which can be measured externally (at least for shallow organs).

FIGURE 2-4 Emission of characteristic x rays occurs when orbital electrons move from an outer shell to fill an inner-shell vacancy. (K_{α} x-ray emission is illustrated.)

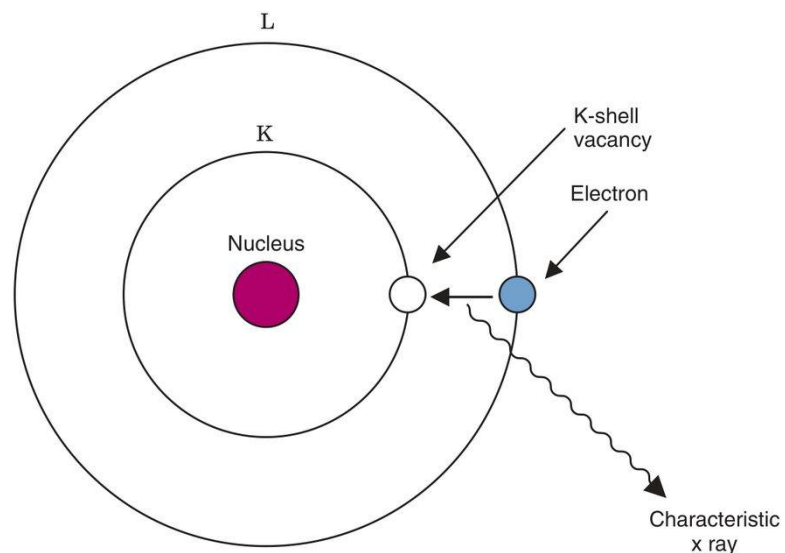


Figure 2-4. CSP 4e, p. 11.

Auger electrons

- **Auger effect:** an outer-shell electron fills the vacancy, but the released energy is **transferred to another orbital electron**, which is **ejected instead of an X-ray**.
- **Kinetic energy** = binding energy of the shell with the original vacancy – sum of the binding energies of the two shells left vacant. For a KLL Auger electron: $E = K_B - 2L_B$.
- Leaves **two vacancies**, which are filled in turn, giving a **cascade** of further X-rays or Auger electrons.

- **Notation e_{abc}** : a = shell with the original vacancy, b = shell the filling electron came from, c = shell the Auger electron left (e.g. e_{KLL}).
- Auger cascades are **low energy with very short range in tissue**, but ionisation density can approach that of an **α -particle track** (high local dose).

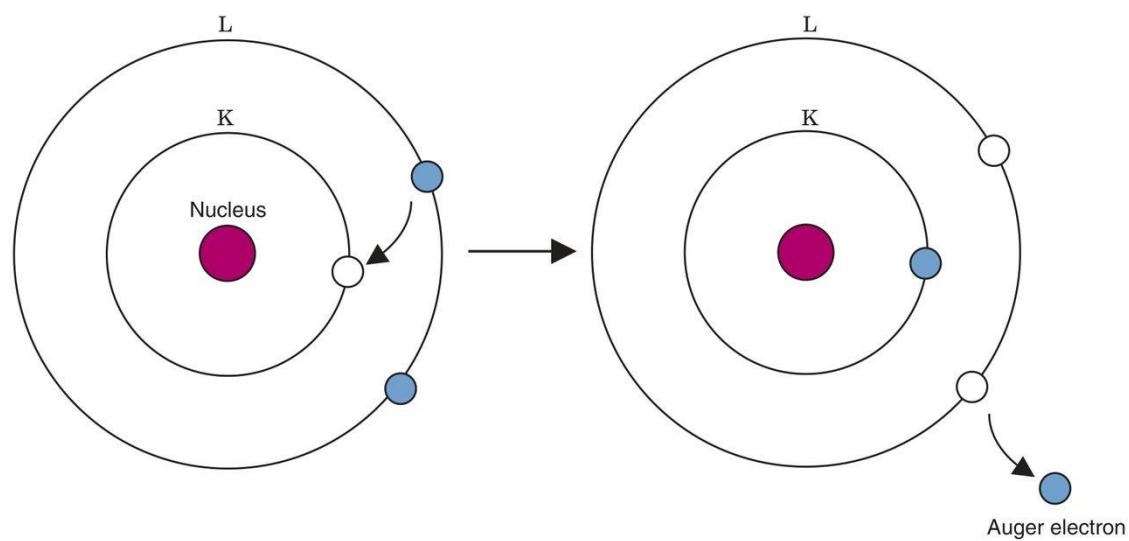


FIGURE 2-5 Emission of an Auger electron as an alternative to x-ray emission. No x ray is emitted.

Figure 2-5. CSP 4e, p. 12.

X-ray versus Auger: fluorescent yield

- **Fluorescent yield (ω_K, ω_L)**: probability that a vacancy yields a characteristic X-ray rather than an Auger electron.
- ω rises with **Z**: **heavy elements mostly emit X-rays; light elements mostly emit Auger electrons**.

Table A2-01.1. Characteristic X-ray vs Auger electron

Feature	Characteristic X-ray	Auger electron
Nature	Photon	Electron
Energy	Difference of two shell binding energies	$K_B - 2L_B$ (KLL)
Vacancies left	One (moves outward)	Two
Favoured in	High-Z atoms (large ω)	Low-Z atoms (small ω)
Range in tissue	Penetrating (if >25 keV, externally detectable)	Very short; dense local ionisation

Pearls

- Both follow an **inner-shell vacancy**: from EC, IC or a particle/photon striking the atom.
- **Auger energy** = $K_B - 2L_B$; X-ray energy = $K_B - L_B$.
- Fluorescent yield $\uparrow$ with Z.
- Tl-201 (EC) emits **69–83 keV X-rays** (93%).

Sources

- CSP 4e, ch. 2 "Basic Atomic and Nuclear Physics", §C.2 and §C.3 "Atomic Emissions", pp. 10–13, Table 2-1, Fig. 2-4 p. 11, Fig. 2-5 p. 12, Fig. 2-6 p. 13; ch. 3, §E–F, pp. 23–24 (IC and EC vacancies; K X-rays >25 keV for $Z \geq 50$).
- SAHA 7e, ch. 2 "Radioactive Decay", §2.1 (Auger process), p. 18; ch. 4, Table 4.1 (Tl-201 X-rays 0.069–0.083 MeV, 93%), p. 71 (second book: K X-ray < K binding energy; Tl-201 example).
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.4 (Auger cascade, ionisation density), p. 37 (second book: Auger ionisation density).

Isomeric transition, internal conversion & electron capture

- › Define and describe with example: i. Isomeric transition, ii. Internal conversion, iii. Electron capture. — Dec 2020 • Paper I • Q2a
 - › Isomeric transition. [3] — Jun 2023 • Paper I • Q7d
 - › Isomeric Transition. [5] — Jun 2025 • Paper I • Q5b
- Asked in: Dec 2020 Paper I Q2a • Jun 2023 Paper I Q7d • Jun 2025 Paper I Q5b

Isomeric transition (IT)

- **Definition:** decay of a **metastable (isomeric) state** of a nucleus by **γ -ray emission**, to a lower-energy state of the same nuclide.
- **Isomers** have the same Z and N (same A) but differ in **energy state and spin** (e.g. **Tc-99m** and **Tc-99**). A metastable state is "long-lived" compared with an ordinary excited state. Lifetimes range from **picoseconds to years**.
- **No change in Z or A:** no transmutation.
- **Example:** **Tc-99m** ($T_{1/2}$ 6 h) $\rightarrow$ **Tc-99** by IT of **140 keV** (142 $\rightarrow$ 140 keV step by internal conversion), with **~10% of transitions by internal conversion**.
- **Importance:** the metastable daughter can be **separated chemically from its parent** in a **generator**, giving a nearly "pure" γ source. Metastable nuclides always emit some conversion electrons, so they are not pure γ emitters.

Fig. 2.5 Decay scheme of ^{99m}Tc illustrating isomeric transition. Ten percent of the decay follows internal conversion

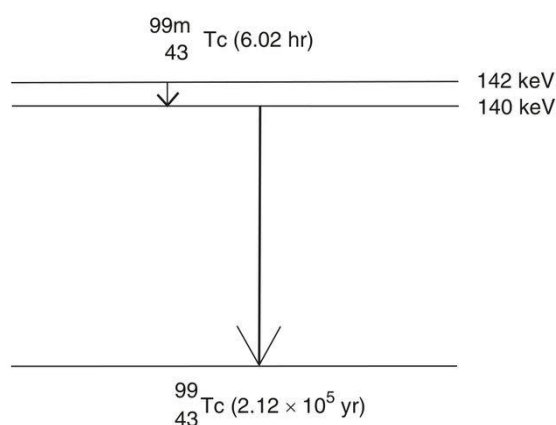


Fig. 2.5. SAHA 7e, p. 17.

Internal conversion (IC)

- **Definition:** an alternative to γ emission. The excited (especially metastable) nucleus **transfers its excitation energy to an orbital electron** (usually K or L), which is **ejected**: the **conversion electron**. It is as if the γ ray were "internally absorbed".
- **Kinetic energy** = $E_\gamma - \text{binding energy of the shell}$ (e.g. $E_\gamma - K_B$); the energy is **discrete**.
- The vacancy is then filled with emission of **characteristic X-rays or Auger electrons**.
- **Conversion coefficient $\alpha = e/\gamma$** (α_K for K-shell): ratio of conversion electrons to γ rays.
- **Versus β^- :** the conversion electron comes from an **orbit**, not the nucleus, and has a **discrete** energy, not a continuous spectrum.
- **Clinical point:** conversion electrons are absorbed locally and **add patient dose**, especially when e/γ is large.

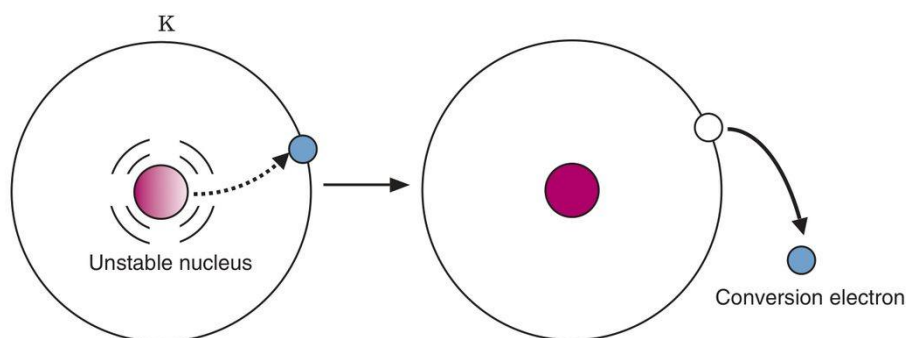


FIGURE 3-5 Schematic representation of internal conversion involving a K-shell electron. An unstable nucleus transfers its energy to the electron rather than emitting a γ ray. Kinetic energy of conversion electron is γ ray energy minus electron-binding energy ($E_\gamma - K_B$).

Figure 3-5. CSP 4e, p. 23.

Electron capture (EC)

- **Definition:** "inverse β^- decay". An **orbital electron (usually K, then L)** is **captured by the nucleus** and combines with a proton to form a neutron: $p + e^- \rightarrow n + \nu + \text{energy}$.
- **Z decreases by 1, A unchanged** (isobaric, transmutation). Drawn "**to the left**" in decay schemes.
- The neutrino carries away energy. The rest appears as **characteristic X-rays and Auger electrons** of the daughter (vacancy filling). EC often leaves the daughter excited, giving **(EC, γ) decay**.
- Occurs in **neutron-deficient** nuclides and **competes with β^+** ; EC is favoured in **heavy elements**, whose orbital electrons lie closer to the nucleus.
- **Examples:** I-125 (EC, γ 35 keV), I-123, Ga-67, In-111, Tl-201, Co-57. F-18 decays **3% by EC** and **97% by β^+** .

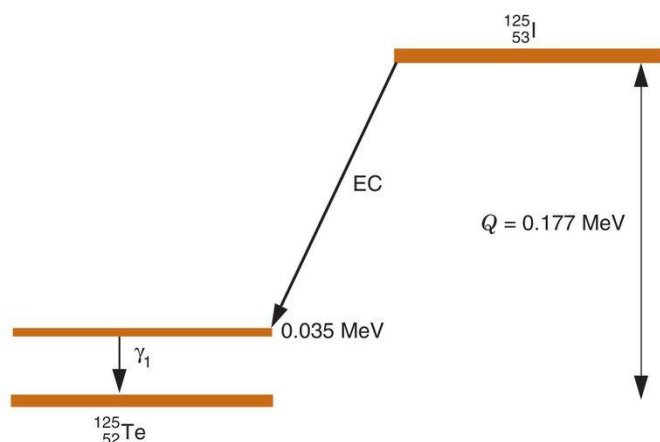


FIGURE 3-6 Decay scheme diagram for ^{125}I , an (EC, γ) emitter.

Figure 3-6. CSP 4e, p. 24.

Table A2-02.1. Comparison

Feature	Isomeric transition	Internal conversion	Electron capture
Change in Z / A	None	None	Z - 1 / A same
Emission	γ ray	Conversion electron (+ X-ray/Auger)	Neutrino + X-rays/Auger ($\pm \gamma$)
Origin of electron	—	Orbital (K/L)	Orbital electron absorbed
Example	Tc-99m (140 keV)	Tc-99m (~10%)	I-125, Tl-201, I-123

Pearls

- IT and IC: **no change in Z**. EC: **Z - 1** (like β^+).
- Conversion electron energy = $E_\gamma - K_B$, discrete.
- EC and IC both end with **X-rays/Auger electrons** from vacancy filling.
- Tc-99m: **IT 140 keV, ~10% by IC**.

Sources

- CSP 4e, ch. 3 "Modes of Radioactive Decay", §E "Isomeric Transition and Internal Conversion", pp. 22–24, Fig. 3-5 p. 23; §F "Electron Capture and (EC, γ) Decay", pp. 24–25, Fig. 3-6 p. 24; §H, p. 26.
- SAHA 7e, ch. 1, §1.3.1 (isomers, lifetimes), p. 8; ch. 2, §2.1 (Tc-99m IT, ~10% IC), p. 17, Fig. 2.5 (second book: Tc-99m IT example and decay-scheme figure).

[2×] A2-03 • 10 marks

I-131 & iodine isotopes — production & decay scheme

- Enumerate different isotopes of Iodine. Describe method of production of ^{131}I . Describe the decay scheme of ^{131}I . [10]

— Jun 2021 • Paper II • Q10

- Decay scheme of I-131. [5] — Jun 2025 • Paper I • Q5a

Asked in: Jun 2021 Paper II Q10 • Jun 2025 Paper I Q5a

Isotopes of iodine used in nuclear medicine

Table A2-03.1. Medical isotopes of iodine (SAHA Table 4.1)

Isotope	$T_{1/2}$	Decay	Main photon (abundance)	Common production
I-123	13.2 h	EC 100%	159 keV (83%)	Cyclotron: $^{121}\text{Sb}(\alpha, 2n)^{123}\text{I}$; $^{124}\text{Te}(\text{p}, 2n)$; via ^{123}Xe (2.1 h)
I-124	4.2 d	β^+ 23%, EC 77%	511 keV (annihilation)	Cyclotron: $^{124}\text{Te}(\text{p}, n)^{124}\text{I}$
I-125	60 d	EC 100%	35 keV (7%); X-rays 27–32 keV	Reactor: $^{124}\text{Xe}(\text{n}, \gamma)^{125}\text{Xe} \rightarrow ^{125}\text{I}$
I-131	8.0 d	β^- 100%	364 keV (81%)	Reactor: fission of U-235; $^{130}\text{Te}(\text{n}, \gamma)^{131}\text{Te} \rightarrow ^{131}\text{I}$

- **Uses:** I-131 for **thyroid cancer therapy and uptake**; I-125 for **biological assays and prostate brachytherapy**; I-124 for **PET imaging of thyroid cancer**; I-123 for **imaging benign thyroid disease and thyroid cancer and for uptake**.
- Iodine has **one stable isotope, I-127**; radioisotopes are known from I-108 to I-147. Besides the four medical isotopes:
 - **I-129** ($T_{1/2}$ about 1.6×10^7 years, β^-): a long-lived fission product, used as a groundwater tracer of nuclear-waste dispersion.
 - **I-132** ($T_{1/2}$ 2.3 h, β^-): a short-lived fission product contributing to early contamination after reactor accidents.
 - **I-126** ($T_{1/2}$ 12.9 d; β^+ and β^- almost equally) and **I-130** ($T_{1/2}$ 12.4 h, β^-): no routine clinical use.

Production of the other iodine isotopes

- **I-123 (cyclotron):**
 - **Direct reactions:** $^{121}\text{Sb}(\alpha, 2n)$, $^{123}\text{Te}(\text{p}, n)$, $^{122}\text{Te}(\text{d}, n)$, $^{124}\text{Te}(\text{p}, 2n)$. The target is dissolved in mineral acid and iodine is distilled into dilute NaOH. These routes may be **contaminated with I-124 and I-125**.
 - **Indirect reactions** produce **Xe-123**, which decays ($T_{1/2}$ 2.1 h) to I-123: $^{122}\text{Te}(\alpha, 3n)$ with 42–46 MeV α ; $^{122}\text{Te}({}^3\text{He}, 2n)$ with 20–30 MeV ${}^3\text{He}$; $^{127}\text{I}(\text{p}, 5n)$ with 60–70 MeV protons.
 - Indirect method: tellurium powder coated inside a **water-cooled chamber**; **helium gas sweeps Xe-123** out of the target. The product is **free of other iodine radioisotopes**.
- **I-124 (cyclotron):** $^{124}\text{Te}(\text{p}, n)^{124}\text{I}$.
- **I-125 (reactor):** $^{124}\text{Xe}(\text{n}, \gamma)^{125}\text{Xe}$; Xe-125 decays by EC ($T_{1/2}$ about 17 h) to I-125.

Production of I-131

- **1. Fission of U-235 in a reactor** (main method):
 - The irradiated target is dissolved in **18% NaOH** by heating; metal hydroxides precipitate on cooling.
 - The **supernatant (sodium iodide)** is acidified with **sulphuric acid** in a closed distillation system. Iodide is oxidised to **iodine**, which is **distilled** and collected in **NaOH** with high radiochemical yield.
 - Supplied as **sodium iodide**, with a reducing agent added to prevent oxidation of iodide to iodine.
- **2. Neutron capture on tellurium:** $^{130}\text{Te}(\text{n}, \gamma)^{131}\text{Te}$; **Te-131 ($T_{1/2}$ 25 min) decays by β^- to I-131**. Product and target are different elements, so I-131 is chemically separated from the tellurium target.
 - Natural tellurium contains about **34% Te-130**, so a natural or enriched tellurium (often tellurium dioxide) target is irradiated in the reactor.

- **Dry distillation:** the irradiated target is heated in a furnace; iodine, with a far higher vapour pressure than tellurium, distils off and is trapped in dilute NaOH. This is now the commonest commercial route.
- **Wet distillation:** the target is dissolved in acid and iodine is distilled from the solution.
- **Fission route:** I-131 is about **2.9% (2.878%) of U-235 thermal-fission products**, so it is recovered in quantity from the fission products; the product is no-carrier-added and of high specific activity.

Decay scheme of I-131

- **I-131 ($T_{1/2}$ 8 d)** decays **100% by β^-** to **stable Xe-131 ($Z + 1$, A unchanged)**.
- β^- branches: **90.4%** to the **364-keV** level, **6.9%** to the **637-keV** level, **1.6%** to the **723-keV** level.
- Principal γ rays: **364 keV (81%)**, **637 keV (7%)**, **284 keV (6%)** (364 $\rightarrow$ 80 keV level); plus an 80-keV transition.
- **$\beta^- E_{\max} = 0.606$ MeV**: responsible for the therapeutic effect and much of the thyroid dose.
- **Mean β energy about 0.19 MeV (192 keV)**; β particles travel **0.6–2 mm in tissue** (maximum about 2 mm in water), so the dose stays within the iodine-concentrating tissue.
- In the main branch (about 89%) the **971 keV total decay energy** is released in two steps: the β^- transition to the 364-keV level of Xe-131, then rapid emission of the 364-keV γ ray.
- The Xe-131 level diagram includes a **metastable state at 0.164 MeV**.

Fig. 2.1 Decay scheme of ^{131}I . Eighty one percent of the total ^{131}I disintegrations decay by 364-keV γ -ray emission. The half-life of ^{131}I is shown in parentheses

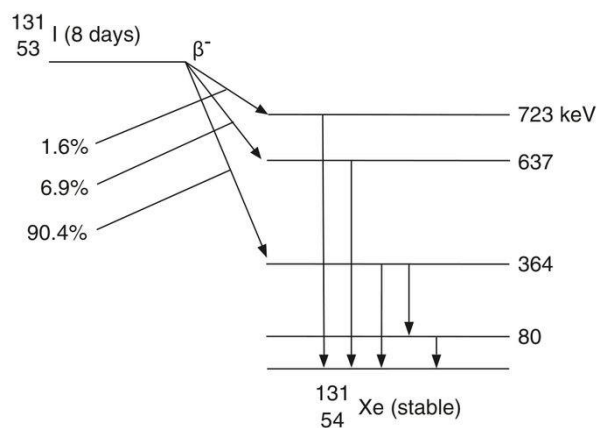
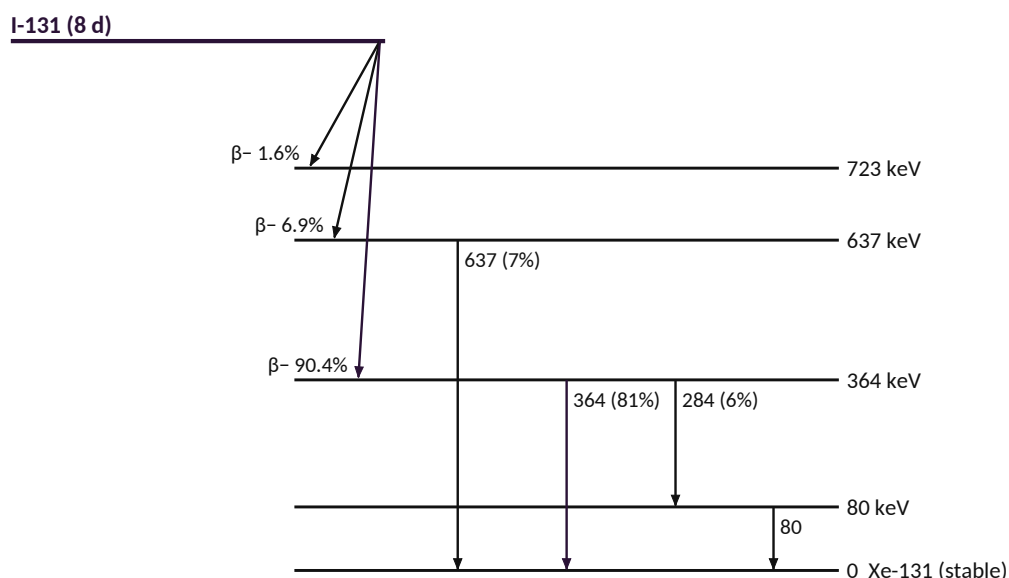


Fig. 2.1. SAHA 7e, p. 13.



Gamma energies in keV with abundance; $\beta^- E_{\max}$ of I-131 = 0.606 MeV (CSP p. 183).

Schematic (exam diagram): decay scheme of I-131 $\rightarrow$ Xe-131 (levels not to scale). Based on SAHA 7e, Fig. 2.1, p. 13; text pp. 13, 61; CSP 4e, Fig. 2-8, p. 15.

- **No change in mass number:** the β^- transformation $n \rightarrow p + e^- + \bar{\nu}$ makes iodine (Z 53) into xenon (Z 54), an **isobaric** transmutation.

- β^- energy is shared randomly with the neutrino, so the **β spectrum is continuous** up to $E_{\max}$, while the γ rays are **discrete lines**.

Practical consequences of the decay scheme

- The **364-keV photon is poor for gamma-camera imaging**: about half penetrate the septa (even with a high-energy collimator) and the 3/8-in. NaI crystal, degrading images.
- **β emission + long half-life** give a high thyroid dose. Diagnostic I-131 doses are therefore limited (10–20 μCi for uptake; 2–3 mCi for cancer imaging, because of **stunning**).
- I-123 (EC, 159 keV, no β) gives roughly **100 times less radiation dose** than I-131 and does not stun, so it has replaced I-131 for diagnostic imaging.
- **Radiation protection**: specific γ -ray constant **0.22 mR/h per mCi at 1 m**; lead **HVL about 0.23 cm**. The 364-keV photons need thick lead shielding of the dispensing area and isolation of therapy patients. The **thyroid is the critical organ** for internal contamination.

Pearls

- I-131: **β^- 100%, 8 d, γ 364 keV (81%), β $E_{\max}$ 0.606 MeV**, daughter **Xe-131 stable**.
- Main β branch **90.4%** feeds the 364-keV level.
- Production: **U-235 fission** (NaOH dissolution, distillation) or $^{130}\text{Te}(n,\gamma) \rightarrow \text{Te-131 (25 min)} \rightarrow \text{I-131}$.
- I-124 = PET iodine (β^+); I-125 = 60 d, low-energy (assays, seeds).

Sources

- SAHA 7e, ch. 4 "Production of Radionuclides", §4.1.2 "Iodine-123", pp. 52–53; §4.2.1 "Fission" (Iodine-131), p. 61; §4.2.2 "Neutron Capture", p. 62; Table 4.1, p. 71.
- SAHA 7e, ch. 2 "Radioactive Decay", §2.1 (β^- decay), pp. 12–13, Fig. 2.1.
- CSP 4e, ch. 2, Fig. 2-8 (^{131}Xe energy levels), p. 15; ch. 12 "Counting Systems", table of β emitters (^{131}I $E_{\beta\max}$ 0.606 MeV), p. 183 (second book: β maximum energy and Xe-131 metastable level).
- REQ 5e, ch. 1 "Radioactivity and Radionuclides", §"Isotopes", e-book PDF p. 27; ch. 8 "Endocrine System", §"Radiopharmaceuticals", e-book PDF pp. 464–465 (second book: clinical uses and imaging limitations).

[2×] A2-04 • 5 marks

Mo-99 / Tc-99m — production & decay scheme

- › Effective dose and equivalent dose – differentiate decay scheme of Mo99. — Jun 2020 • Paper I • Q1
- › Production and decay scheme of Tc-99m. [5] — Dec 2024 • Paper I • Q5b

Asked in: Jun 2020 Paper I Q1 • Dec 2024 Paper I Q5b

Production of Mo-99 (parent of Tc-99m)

- **Fission of U-235** (the main route): about **6% of fission products are Mo-99**. Target irradiated at $\sim 10^{14}$ n/cm²·s for 5–7 days, cooled, dissolved (NaOH or HNO₃), Mo adsorbed on alumina, eluted with NH₄OH and purified.
- Gives **high specific activity**. All current generators use **fission Mo-99**.
- **Neutron capture**, $^{98}\text{Mo}(n,\gamma)^{99}\text{Mo}$ ("irradiated molybdenum"): specific activity **too low** for the generator.
- LEU (<20% U-235) targets are being adopted in place of HEU for supply security.

Production of Tc-99m: the Mo-99/Tc-99m generator

- **Alumina (Al₂O₃) column** (5–10 g) holds Mo-99 as **molybdate (MoO₄²⁻)**. **0.9% NaCl elutes Tc-99m as pertechnetate (TcO₄⁻)**.
- Half-lives differ by a factor of about 11. Tc-99m reaches **maximum about 24 h** (≈ 4 half-lives) after elution, then follows Mo-99 decay (**transient equilibrium**). Elution yield is **80%–90%**.
- The column is shielded with lead, or depleted uranium for high-activity generators.

Decay schemes

- **Mo-99 (T_{1/2} 66 h)** decays by β^- : **82%** to the 142-keV level (**Tc-99m**), **17%** to 922 keV, plus minor branches (0.3%, <1%).
- Mo-99 photons: **740 and 780 keV** (used to detect breakthrough) and 181 keV.
- About **87%** of Mo-99 decays end in **Tc-99m**; **13%** go directly to Tc-99.

- **Tc-99m ($T_{1/2}$ 6 h)** decays by **isomeric transition**: 142 $\rightarrow$ 140 keV (2 keV, by internal conversion), then the **140-keV γ (90% yield)**. About **10%** of transitions are by **internal conversion**. No change in Z.
- **Tc-99 ($T_{1/2}$ 2.1×10^5 y)** decays by β^- to **stable Ru-99**.

Fig. 2.2 Decay scheme of ^{99}Mo . There is a 2-keV isomeric transition from the 142-keV level to the 140-keV level, which occurs by internal conversion. Approximately 87% of the total ^{99}Mo ultimately decays to $^{99\text{m}}\text{Tc}$, and the remaining 13% decays to ^{99}Tc . (The energy levels are not shown in scale.)

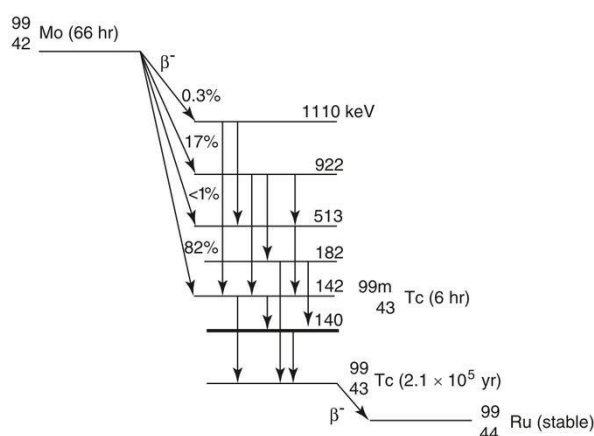
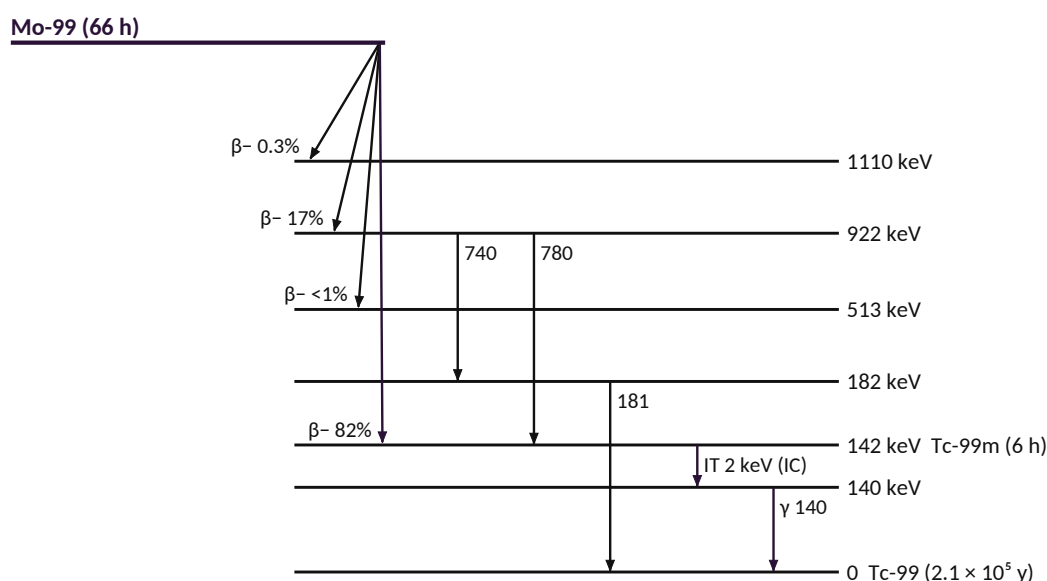


Fig. 2.2. SAHA 7e, p. 13.



Gamma energies in keV; Tc-99 decays by β^- to stable Ru-99. About 87% of Mo-99 decays reach Tc-99m (SAHA p. 13).

Schematic (exam diagram): decay scheme of $^{99}\text{Mo} \rightarrow ^{99\text{m}}\text{Tc} \rightarrow ^{99}\text{Tc}$ (levels not to scale). Based on SAHA 7e, Fig. 2.2, p. 13 and Fig. 2.5, p. 17; text pp. 13, 17, 70, 86.

Pearls

- Tc-99m: **6 h, 140 keV (90%), IT, little electron emission**, nearly ideal for gamma cameras.
- Generator: **fission Mo-99 on alumina, saline elution, maximum Tc-99m at ~24 h**.
- Breakthrough is detected through the **740/780-keV Mo-99 photons**.

Sources

- SAHA 7e, ch. 2 "Radioactive Decay", §2.1, p. 13, Fig. 2.2; p. 17, Fig. 2.5.
- SAHA 7e, ch. 4 "Production of Radionuclides", §4.2.1 "Fission or (n, f) Reaction" (Molybdenum-99), pp. 60–61; §4.2.2 "Neutron Capture", p. 62; Table 4.1, p. 70.
- SAHA 7e, ch. 5 "Radionuclide Generators", §5.2.1 " ^{99}Mo – $^{99\text{m}}\text{Tc}$ Generator", pp. 79–80; Fig. 5.2, p. 80.

Modes of radioactive decay

- Write various modes of decay of radionuclides and describe principle of decay mode underlying the positron emission tomography. [10] — Jun 2021 • Paper I • Q9
 - Describe different types of radioactive decay schemes with suitable examples. [10] — Dec 2022 • Paper I • Q1
- Asked in: Jun 2021 Paper I Q9 • Dec 2022 Paper I Q1

General concepts

- Radioactive decay:** an unstable nucleus transforms into a more stable one by emitting particles, photons or both, **converting mass into energy** (transition energy Q). It is **spontaneous** and unaffected by chemical state.
- Decay scheme diagram:** the parent line is drawn above the daughter. **Vertical distance $\propto$ transition energy**. Decay is drawn **to the right if Z increases** and **to the left if Z decreases**; γ transitions (no change in Z) are drawn vertically.
- The mode chosen depends on position relative to the **line of stability**: neutron-rich nuclides decay by β^- ; neutron-deficient ones by **EC or β^+** ; very heavy ones by α or fission.

FIGURE 3-9 Decay scheme diagram for ^{18}F , which decays by both electron capture and β^+ emission competitively.

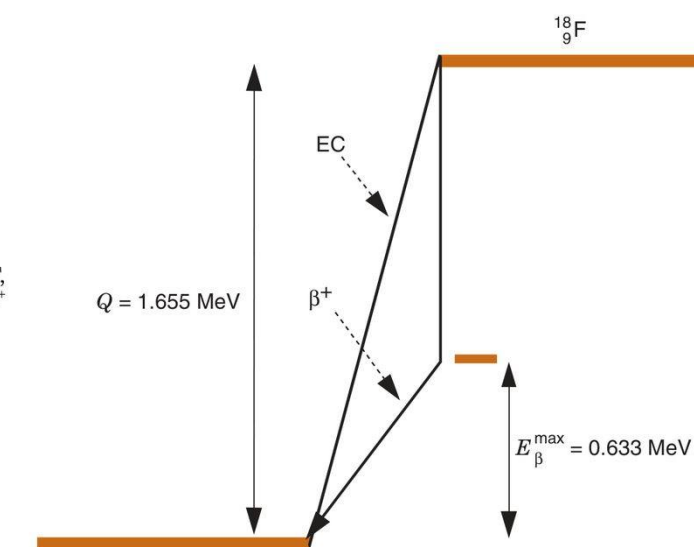
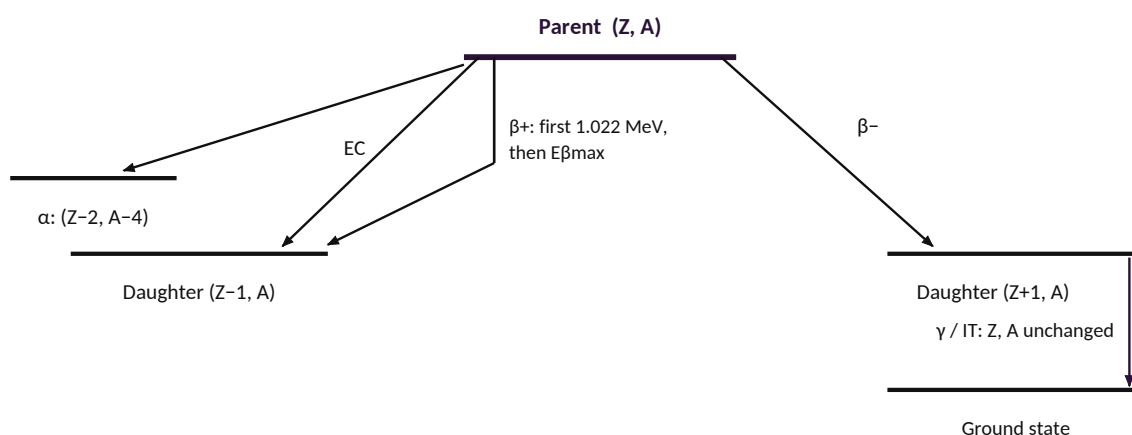


Figure 3-9. CSP 4e, p. 27.



Vertical distance proportional to transition energy; Z increases left $\rightarrow$ right

Schematic (exam diagram): conventions of decay-scheme diagrams for the main decay modes. Based on CSP 4e, Fig. 3-1, p. 20, Fig. 3-8, p. 26 and Fig. 3-9, p. 27; text pp. 19–27.

Modes of decay with examples

Table A2-05.1. Decay modes

Mode	Nuclear change	Z / A	Examples
β^-	$n \rightarrow p + e^- + \bar{\nu}$; continuous β spectrum (mean $\approx \frac{1}{3}E_{\beta\max}$)	Z+1 / same	C-14, P-32, H-3 (pure β^-)
(β^-, γ)	β^- to an excited daughter, then γ	Z+1 / same	I-131, Xe-133, Cs-137
IT / IC	Metastable state emits γ or conversion electron	same / same	Tc-99m
EC, (EC, γ)	$p + e^- \rightarrow n + \nu$; X-rays/Auger	Z-1 / same	I-123, I-125, Ga-67, In-111, Tl-201
β^+	$p \rightarrow n + e^+ + \nu$; needs ≥ 1.022 MeV	Z-1 / same	N-13, O-15 (pure β^+)
β^+ / EC competitive	Both modes	Z-1 / same	F-18 (97% β^+ , 3% EC), C-11
α	Emits He-4 nucleus (4–8 MeV, ~ 0.03 mm in tissue)	Z-2 / A-4	Ra-226, Am-241
Fission	Splits $\sim 60:40$ + 2–3 neutrons, hundreds of MeV	—	U-235 (reactor)

β^- decay

- A neutron becomes a proton + electron (β^- particle) + (anti)neutrino. Energy is shared randomly, so the **β spectrum is continuous** up to $E_{\beta\max} = Q$; mean energy $\approx \frac{1}{3} E_{\beta\max}$ (C-14: 0.156 and 0.0497 MeV).
- β particles penetrate only a few mm of tissue, so **pure β^- emitters are rarely used for in-vivo measurement** (they suit therapy).
- In **(β^-, γ)** decay the daughter is formed in an excited state and emits **discrete γ rays**, which suit imaging.
- Example of **(β^-, γ)** : **Xe-133**, where 99.3% of decays go by one β branch to the 0.081-MeV level of Cs-133, followed by the 81-keV γ ray or conversion electrons.
- Transition energy is defined from **atomic** masses, because both nuclear and orbital-electron mass can be converted into energy.

Electron capture and isomeric transition

- EC**: orbital (K/L) electron captured; Z - 1; characteristic X-rays and Auger electrons follow. It is favoured over β^+ in heavy elements.
- IT**: metastable daughter decays by γ (or internal conversion) with **no change in Z or A**. Metastable daughters can be separated in **generators** (Tc-99m).

Positron (β^+) decay: the decay mode underlying PET

- A proton becomes a neutron + **positron** + neutrino; Z - 1. The transition needs **at least 1.022 MeV** (2×511 keV electron rest masses); the excess is shared as $E_{\beta\max}$.
- The positron loses its energy and comes to rest **within a few millimetres** in tissue. It briefly forms **positronium** ($\sim 10^{-10}$ s) and **annihilates** with an electron.
- Annihilation produces **two 511-keV photons emitted back-to-back ($\sim 180^\circ$)**; slight non-collinearity (a few tenths of a degree) occurs because the pair is moving.
- Principle of PET (annihilation coincidence detection)**: two photons per decay, emitted **simultaneously in opposite directions**. Near-simultaneous detection in two opposing detectors **localises the annihilation along the line between them**, without absorptive collimators. A coincidence time stamp precision of about **1–2 ns** is typical.
- PET nuclides: **F-18 (97% β^+)**, **C-11**, **N-13**, **O-15**.

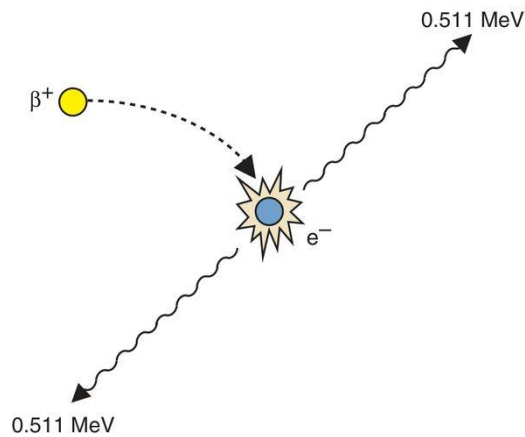


FIGURE 3-7 Schematic representation of mutual-annihilation reaction between a positron (β^+) and an ordinary electron. A pair of 0.511-MeV annihilation photons are emitted “back-to-back” at 180 degrees to each other.

Figure 3-7. CSP 4e, p. 25.

Competitive β^+ / EC decay

- β^+ and EC have the **same effect on the nucleus** ($Z - 1$, isobaric) and are alternative routes to the same daughter.
- **β^+ predominates in lighter elements; EC in heavier elements**, because their orbital electrons lie closer to the nucleus and are more easily captured.
- If $Q < 1.022$ MeV only EC is possible. Example: **F-18** (Q 1.655 MeV, $E_{\beta_{\max}}$ 0.633 MeV): 97% β^+ , 3% EC.
- Some odd–odd nuclides near the line of stability decay **both ways**: **K-40** (89% β^- , 11% EC or β^+).

α decay and fission

- **α** : very heavy nuclides that must lose mass; $A - 4$, $Z - 2$; not isobaric. α energies are **4–8 MeV**, but the range is only about **0.03 mm** in tissue, giving large local doses.
- Natural **decay series**: U-238 $\rightarrow$ Pb-206 (“ $4n + 2$ ”), U-235 $\rightarrow$ Pb-207 ($4n + 3$), Th-232 $\rightarrow$ Pb-208 ($4n$). The $4n + 1$ series has died out. Ra-226 and Rn-222 belong to the U-238 series.
- **Am-241** (α , γ) serves as a 60-keV calibration source.
- **Fission**: a very heavy nucleus splits into two fragments (about 60:40) plus 2–3 neutrons, releasing hundreds of MeV. It powers reactors; its **radioactive fragments** (e.g. Mo-99, I-131) are separated for medical use, and the **neutrons** produce radionuclides by activation.

Pearls

- $\beta^- \rightarrow$ **right** ($Z + 1$); EC/ $\beta^+ \rightarrow$ **left** ($Z - 1$); γ /IT $\rightarrow$ **vertical** (Z unchanged).
- β^+ needs **≥ 1.022 MeV**; $E_{\beta_{\max}} = Q - 1.022$ MeV (O-15: Q 2.722, $E_{\beta_{\max}}$ 1.7 MeV).
- PET = **two 511-keV photons at $\sim 180^\circ$** , detected in coincidence.
- β spectra are **continuous**; γ , conversion-electron and X-ray energies are **discrete**.

Sources

- CSP 4e, ch. 3 “Modes of Radioactive Decay”, §A–J, pp. 19–28: β^- (Fig. 3-1, 3-2, pp. 20–21), (β^- , γ) pp. 21–22, IT/IC pp. 22–24, EC p. 24, β^+ and annihilation pp. 25–26 (Fig. 3-7, 3-8), competitive β^+ /EC (Fig. 3-9, p. 27), α and fission pp. 26–28, line of stability p. 28.
- CSP 4e, ch. 18 “Positron Emission Tomography”, §A.1 “Annihilation Coincidence Detection”, p. 307.

[1×] A2-06 • 2 marks

Define the following: Branching Ratio.

Asked in: Dec 2020 Paper I Q9e

Definition

- Some radionuclides decay by **more than one mode** ("branching" decay). Each mode i has its own **partial decay constant** λ_i , and the total decay constant is their sum:

$$\lambda = \lambda_1 + \lambda_2 + \lambda_3 + \dots \quad \text{B.R.}_i = \lambda_i / \lambda$$

- Branching ratio (B.R.):** the fraction of nuclei decaying by a specific mode (or to a specific daughter state).

Examples

- F-18:** 97% β^+ , 3% EC (B.R. for β^+ = 0.97).
- Mo-99 $\rightarrow$ Tc-99m:** B.R. = **0.876**. The rest bypass the metastable state and go directly to Tc-99. Tc-99m activity in a generator is therefore the Bateman value $\times$ 0.876; the transient-equilibrium Tc-99m/Mo-99 ratio is about **0.96**.

Use

- Appears in the **Bateman (parent–daughter) equation** and in the equilibrium ratio $A_d/A_p = [T_p/(T_p - T_d)] \times \text{B.R.}$

Pearls

- B.R. = λ_i/λ ; partial constants add.
- Mo-99 $\rightarrow$ Tc-99m B.R. **0.876**; F-18 β^+ **0.97**.

Sources

- CSP 4e, ch. 4 "Decay of Radioactivity", §A.1 "The Decay Constant", p. 31, Eq. 4-2, 4-3; §G.1–3 (Bateman equation, B.R. 0.876), pp. 40–41, Eq. 4-25, 4-27.
- CSP 4e, ch. 5, §C "Radionuclide Generators", p. 51 (B.R. 0.876, ratio $\approx$ 0.96).

A3 Decay equation & half-lives

[4×+] A3-01 • 10 marks

Decay equation ($N = N_0 e^{-\lambda t}$), half-life & mean life

- Derive decay equation. What are the different types of equilibrium achieved in a mixture of parent and daughter radionuclides? — Dec 2020 • Paper I • Q8
- a) What is radioactive decay? [2] b) Derive the equation: $n = n_0 e^{-\lambda t}$. Also derive the equation for half-life, and average life of radioactivity. [8] — Dec 2021 • Paper I • Q9a–b
- Derive the expression $N = N_0 e^{-\lambda t}$. [5] — Dec 2023 • Paper I • Q2a
- Derive radionuclide decay equation. [10] — Jun 2024 • Paper I • Q5

Asked in: Dec 2020 Paper I Q8 • Dec 2021 Paper I Q9a–b • Dec 2023 Paper I Q2a • Jun 2024 Paper I Q5

What is radioactive decay?

- A process in which an **unstable nucleus transforms into a more stable one** by emitting particles, photons or both, **releasing energy (mass $\rightarrow$ energy)**.
- It is **spontaneous and random**: the moment a given nucleus decays cannot be predicted, and it is essentially unaffected by chemical or physical conditions. Only **average decay rates** can be described, in terms of probability.
- Decay constant (λ)**: the fraction of atoms decaying per unit time, i.e. the **probability that an atom decays per unit time**. Units: time^{-1} ($\lambda = 0.01 \text{ s}^{-1} \rightarrow 1\% \text{ decays each second}$).
- Activity A** = number of disintegrations per unit time = λN . SI unit **becquerel (1 Bq = 1 dps)**; traditional unit **curie (1 Ci = 3.7×10^{10} dps)**, so 1 mCi = 37 MBq.

Derivation of the decay equation $N = N_0 e^{-\lambda t}$

- The rate of decay is proportional to the number of radioactive atoms present:

$$dN/dt = -\lambda N \quad (\text{the minus sign: } N \text{ decreases with time})$$

- Separate the variables and integrate from $t = 0$ ($N = N_0$) to t ($N = N_t$):

$$\int dN/N = -\lambda \int dt \quad \ln N_t - \ln N_0 = -\lambda t \quad \ln (N_t/N_0) = -\lambda t$$

$$N_t = N_0 e^{-\lambda t} \text{ and, since } A = \lambda N, A_t = A_0 e^{-\lambda t}$$

- $e^{-\lambda t}$ is the **decay factor (DF)**: the fraction of atoms (or activity) remaining after time t .
- For small exponents ($\lambda t \approx 0.1$), $e^{-\lambda t} \approx 1 - \lambda t$.
- Decay factors come from **tables** (e.g. Tc-99m, DF after 6 h = 0.5), a **calculator**, or a **universal decay curve**. For a **pre-calibrated** shipment (activity stated for a future time), use a negative t : $DF(-t) = 1/DF(t)$.
- The equation predicts only the **average** decay rate; actual counts fluctuate statistically from moment to moment.
- Exponential decay removes a **constant fraction per unit time**. It is a curve on a linear plot and a **straight line on a semilogarithmic plot** (slope = $-\lambda$).

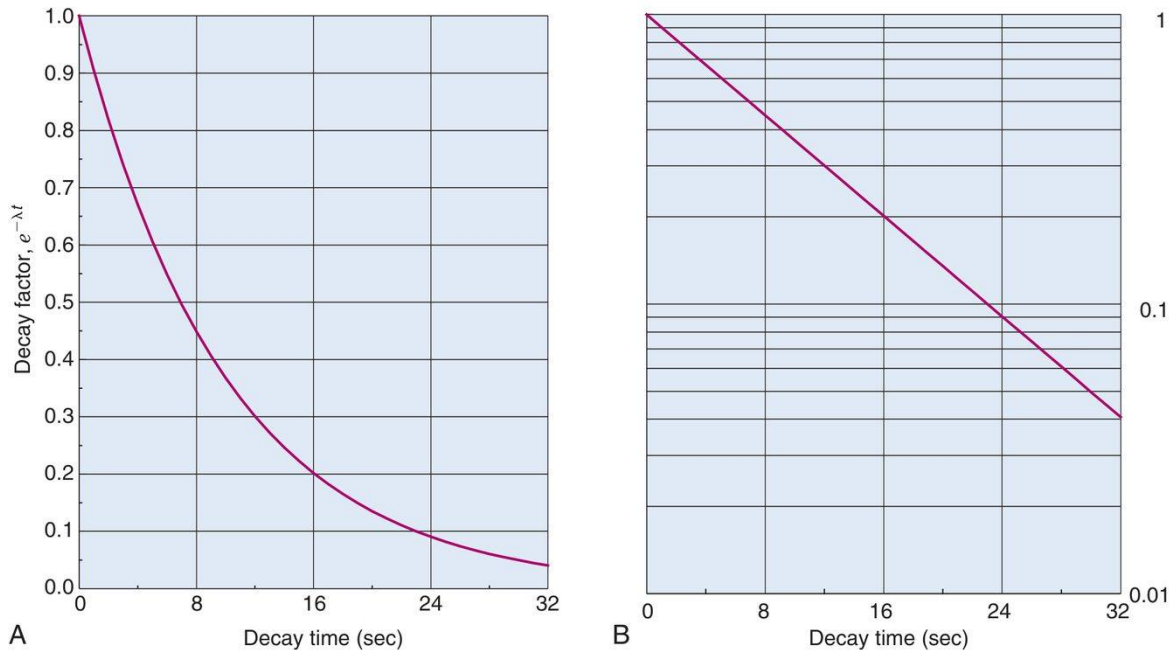


FIGURE 4-2 Decay factor versus time shown on linear (A) and semilogarithmic (B) plots, for radionuclide with $\lambda = 0.1 \text{ sec}^{-1}$.

Figure 4-2. CSP 4e, p. 33.

Derivation of half-life ($T_{1/2}$)

- **Definition:** the time for the activity (or number of atoms) to fall to **50%** of its initial value; unique to each radionuclide.
- Put $N_t = N_0/2$ at $t = T_{1/2}$:

$$\frac{1}{2} = e^{-\lambda T_{1/2}} \quad 2 = e^{\lambda T_{1/2}} \quad \ln 2 = \lambda T_{1/2}$$

$$T_{1/2} = \ln 2 / \lambda = 0.693 / \lambda \quad \lambda = 0.693 / T_{1/2}$$

- After n half-lives: $A_t = A_0/2^n$, with $n = t/T_{1/2}$.
- $T_{1/2}$ is found experimentally from the slope of a semilog plot of activity against time.

Derivation of average (mean) life (τ)

- **Mean life:** the average lifetime of the atoms in a sample (individual atoms live from "very short" to "very long").
- Average of t weighted by the decay probability at time t :

$$\tau = \int_0^\infty t e^{-\lambda t} dt / \int_0^\infty e^{-\lambda t} dt = (1/\lambda^2) / (1/\lambda) = 1/\lambda$$

$$\tau = T_{1/2} / \ln 2 = 1.44 T_{1/2}$$

- In one mean life, activity falls to $e^{-1} \approx 37\%$ of its initial value.
- Mean life is important in **radiation dosimetry** calculations.

Worked example — Decay of a sample (SAHA values)

- A sample of 250 mCi (9.25 GBq), $T_{1/2} = 10$ days. Activity after 23 days?
- $n = 23/10 = 2.3$ half-lives; $A = 250/2^{2.3} = 250/4.92 = 50.8 \text{ mCi (1.88 GBq)}$.
- Same by the decay equation: $\lambda = 0.693/10 \text{ d} = 0.0693 \text{ d}^{-1}$; $A = 250 \times e^{-0.0693 \times 23} = 50.8 \text{ mCi}$.

Types of equilibrium in a parent-daughter mixture (see A4-01)

Table A3-01.1. Parent-daughter equilibria

Type	Condition	Example
Secular	$T_p \gg T_d$ (factor > 100); $A_d = A_p$ after $\sim 5 T_d$	Ra-226 $\rightarrow$ Rn-222; Cs-137 $\rightarrow$ Ba-137m; Sn-113 $\rightarrow$ In-113m
Transient	$T_p > T_d$ (factor ~ 10 –50); daughter decays with T_p , $A_d/A_p = T_p/(T_p - T_d)$	Mo-99 $\rightarrow$ Tc-99m
No equilibrium	$T_d > T_p$	Te-131m $\rightarrow$ I-131

Pearls

- $A = \lambda N$; $N = N_0 e^{-\lambda t}$; $T_{1/2} = 0.693/\lambda$; $\tau = 1/\lambda = 1.44 T_{1/2}$.
- After one mean life 37% remains; after one half-life 50%.
- Semilog plot of activity vs time: a straight line with slope $-\lambda$.
- 1 Ci = 3.7×10^{10} Bq; 1 mCi = 37 MBq.

Sources

- CSP 4e, ch. 4 "Decay of Radioactivity", §A.1 "The Decay Constant" and §A.2 "Definition and Units of Activity", pp. 31–32, Eq. 4-1 to 4-6 (with derivation 4-6a–c); §B.1–3 "Decay Factor", "Half-Life", "Average Lifetime", pp. 32–34, Eq. 4-7 to 4-12, 4-11a; §C.1–3 (tables, pre-calibrated shipments), pp. 34–35; Fig. 4-2, p. 33; ch. 3, §A, p. 19.
- CSP 4e, ch. 4, §G.2–4 "Secular Equilibrium", "Transient Equilibrium", "No Equilibrium", pp. 40–41.
- SAHA 7e, ch. 2 "Radioactive Decay", §2.2.1–2.2.3, pp. 18–21 (37% after one mean life; worked example, p. 20); §2.3.2–2.3.3, pp. 24–26 (half-life ratio factors 10–50 and >100) (second book: worked example, 37% rule and ratio criteria).

[2×] A3-02 • 5 marks

Physical, biological & effective half-life

- › Physical half life, Effective half life and Biological half life. [3] — Jun 2022 • Paper I • Q10a
- › Describe physical half life, biological half life and effective half life and their clinical implications. [5] — Jun 2025 • Paper I • Q1a

Asked in: Jun 2022 Paper I Q10a • Jun 2025 Paper I Q1a

Physical half-life (T_p)

- **Time for a radionuclide to decay to 50% of its initial activity**; a fixed property of the nuclide.

$$T_{1/2} = \ln 2 / \lambda \approx 0.693 / \lambda ; A(t) = A(0) e^{-\lambda t}$$

- **Average lifetime** $\tau = 1/\lambda = T_{1/2} / \ln 2 \approx 1.44 T_{1/2}$; used in dosimetry.

Biological half-life (T_b)

- The rate of **clearance of the radiopharmaceutical from the body** (or organ) by physiological excretion.
- Often **multi-exponential**: fraction f_1 cleared with T_{b1} , f_2 with T_{b2} , and so on.

Effective half-life (T_e)

- When clearance is by both physical decay and a single-component biological excretion, the total clearance is one exponential with half-life T_e . Excretion acts like a **second "branch" of decay**.

$$1/T_e = 1/T_p + 1/T_b \quad T_e = (T_p \times T_b) / (T_p + T_b)$$

- T_e is always **shorter than both** T_p and T_b . If $T_p \gg T_b$, clearance is effectively biological only ($T_e \approx T_b$).

Table A3-02.1. Comparison

Feature	Physical	Biological	Effective
Determined by	The nuclide (decay constant λ)	Physiological clearance of the compound	Both
Use	Decay correction, dispensing	Kinetics	Dose (cumulated activity)

Clinical implications

- **Radiation dose**: cumulated activity $\tilde{A} \approx 1.44 \times T_e \times A_0$, so the dose to a source organ scales with T_e .

- **Choice of radionuclide:** T_p should be seconds to days, preferably **minutes to hours**, and long enough for the biological process. **Labelled antibodies** need hours to days; minute-lived labels are useless there.
- **Imaging counts:** T_p and T_b together set the number of decays seen from a region over time.
- **Dispensing:** decay factors from T_p give the volume to draw for a later injection (e.g. Tc-99m DF after 8 h = 0.397).

Worked example — Effective half-life and cumulated activity: I-131 in the thyroid (CSP Example 22-9 values)

- Given: $T_p = 8$ d, $T_b = 2$ d, thyroid uptake 60%.
- $T_e = (8 \times 2)/(8 + 2) = 16/10 = 1.6$ d ($= 1.38 \times 10^5$ s).
- $\tilde{A}$ per MBq given $= 1.44 \times 1.38 \times 10^5 \text{ s} \times 0.60 \times 1 \text{ MBq} = 1.19 \times 10^5 \text{ MBq}\cdot\text{s per MBq}$.
- Without excretion ($T_e = T_p = 8$ d), $\tilde{A}$ would be 5 times larger (8/1.6): **biological clearance cuts the thyroid dose by 80%.**

Pearls

- $1/T_e = 1/T_p + 1/T_b$, not $T_e = T_p + T_b$ (exam trap).
- $T_e < \text{the shorter of } T_p \text{ and } T_b$.
- $\tau = 1.44 T_{1/2}$; $\tilde{A} = 1.44 T_e A_0$.

Sources

- CSP 4e, ch. 4 "Decay of Radioactivity", §B.2 "Half-Life" and §B.3 "Average Lifetime", pp. 33–34, Eq. 4-8 to 4-12, Example 4-1.
- CSP 4e, ch. 5 "Radionuclide and Radiopharmaceutical Production", §E "Radiopharmaceuticals" (half-life choice, biologic half-life), pp. 57, 59.
- CSP 4e, ch. 22 "Internal Radiation Dosimetry", §B.2 "Cumulated Activity", pp. 410–412, Eq. 22-8 to 22-11; Example 22-9, p. 416.
- SAHA 7e, ch. 6, §6.2.2 "Short Effective Half-Life", p. 95 (second book: explicit statement that T_e is shorter than both T_p and T_b).

A4 Radioactive equilibrium

[4x+] A4-01 · 10 marks

Transient & secular equilibrium

- › Transient and secular equilibrium – concept, examples and relevance in nuclear medicine practice. — Jun 2020 · Paper I · Q2
- › Derive decay equation. What are the different types of equilibrium achieved in a mixture of parent and daughter radionuclides? — Dec 2020 · Paper I · Q8
- › Discuss transient and secular equilibrium – concept, examples and relevance in nuclear medicine practice. [10] — Dec 2022 · Paper II · Q8
- › What is radioactive equilibrium? Discuss about the different types of radioactive equilibrium with the implications in routine clinical practice. [10] — Dec 2023 · Paper I · Q3
- › Transient and secular equilibrium. [5] — Jun 2025 · Paper I · Q9b

Asked in: Jun 2020 Paper I Q2 · Dec 2020 Paper I Q8 · Dec 2022 Paper II Q8 · Dec 2023 Paper I Q3 · Jun 2025 Paper I Q9b

Concept: parent–daughter (Bateman) relationship

- When a radioactive **parent (p)** decays to a radioactive **daughter (d)**, the daughter is **formed and decays at the same time**:

$$dN_p/dt = -\lambda_p N_p \quad dN_d/dt = \lambda_p N_p - \lambda_d N_d$$

- Solving (Bateman equation, initial daughter activity $A_d(0)$):

$$A_d(t) = A_p(0) \cdot [\lambda_d/(\lambda_d - \lambda_p)] \cdot (e^{-\lambda_p t} - e^{-\lambda_d t}) \cdot \text{B.R.} + A_d(0) e^{-\lambda_d t}$$

- **B.R.** = branching ratio to the daughter of interest (0.876 for Mo-99 → Tc-99m).
- **Radioactive equilibrium:** after enough time, the **ratio of daughter to parent activity becomes constant**. Which type is reached depends on the relative half-lives.

Secular equilibrium

- **Condition:** $T_p \gg T_d$ (parent decay negligible over the observation period; half-lives differ by a **factor > 100**); $\lambda_p \approx 0$:

$$A_d(t) \approx A_p(0) (1 - e^{-\lambda_d t}) \times \text{B.R.}$$

- Daughter activity is $\approx \frac{1}{2} A_p$ after $1 T_d$, $\approx \frac{3}{4} A_p$ after $2 T_d$, and **equals the parent ($A_d \approx A_p \times \text{B.R.}$) after about $5 T_d$** . Both then decay with the **parent's half-life**.

- **Examples:** Ra-226 (1620 y) → Rn-222 (4.8 d); Cs-137 (30 y) → Ba-137m (2.6 min); Sn-113 (117 d) → In-113m (100 min). Generators: **Ge-68 (271 d) → Ga-68 (68 min)** and **Sr-82 (25 d) → Rb-82 (1.3 min)** (from the half-life ratio).

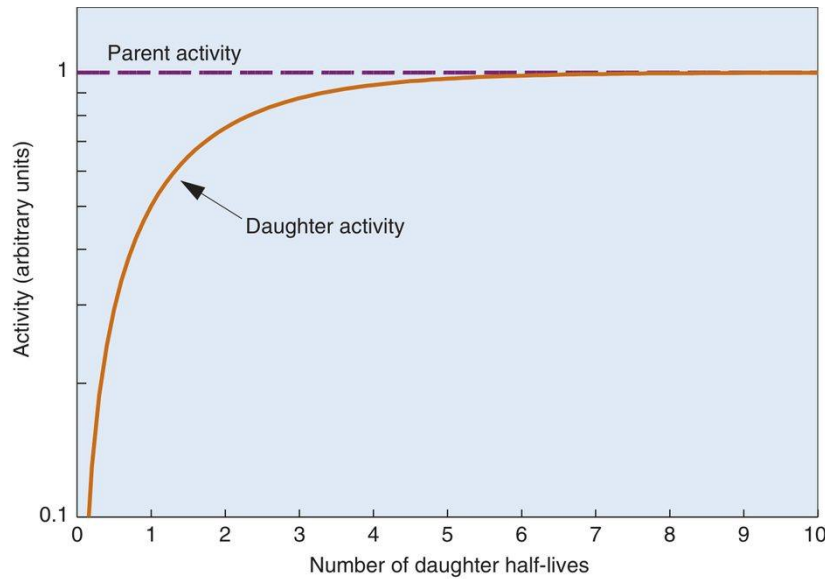


FIGURE 4-7 Buildup of daughter activity when $T_d \ll T_p \approx \infty$, branching ratio = 1. Eventually, secular equilibrium is achieved.

Figure 4-7. CSP 4e, p. 40.

Transient equilibrium

- **Condition:** $T_p > T_d$ but not "infinite" (half-lives differ by a **factor of about 10–50**).
- Daughter activity **rises, exceeds the parent (if B.R. = 1), reaches a maximum, then decays with the parent's half-life**. The curves become parallel at a constant ratio:

$$A_d/A_p = [T_p/(T_p - T_d)] \times \text{B.R.}$$

$$t_{\max} = 1.44 \times [T_p T_d / (T_p - T_d)] \times \ln(T_p/T_d)$$

- **Example: Mo-99 (66 h) → Tc-99m (6 h).** Because B.R. = 0.876 (87% of Mo-99 decays reach Tc-99m), **Tc-99m activity stays slightly below Mo-99**. The maximum is reached in **about 23 h (~4 Tc-99m half-lives)**.

Fig. 2.9 Plot of logarithm of ^{99}Mo and $^{99\text{m}}\text{Tc}$ activities versus time showing transient equilibrium. The activity of the daughter $^{99\text{m}}\text{Tc}$ is less than that of the parent ^{99}Mo , because only 87% of ^{99}Mo decays to $^{99\text{m}}\text{Tc}$ radionuclide. If 100% of the parent were to decay to the daughter, then the daughter activity would be higher than the parent activity after reaching equilibrium, as recognized from Eq. (2.12)

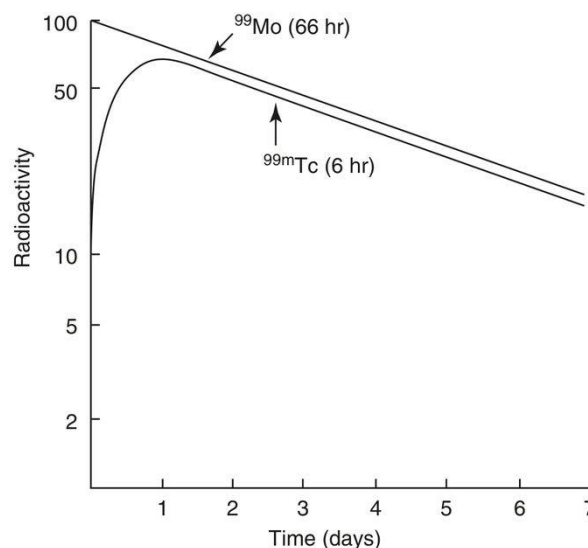


Fig. 2.9. SAHA 7e, p. 25.

Worked example — Mo-99/Tc-99m generator (book data)

- $T_p = 66 \text{ h}$, $T_d = 6 \text{ h}$, B.R. = 0.876.
- $t_{\max} = 1.44 \times (66 \times 6/60) \times \ln(66/6) = 1.44 \times 6.6 \times 2.398 = \mathbf{22.8 \text{ h} \approx 23 \text{ h}}$.
- Equilibrium ratio $A_{\text{Tc}}/A_{\text{Mo}} = (66/60) \times 0.876 = 1.10 \times 0.876 = \mathbf{0.96}$.

No equilibrium

- **Condition:** $T_d > T_p$. Daughter activity rises to a maximum ($t_{\max}$ by the same equation), then, once the parent has gone, decays with its **own** half-life. The curves never become parallel.
- **Example:** Te-131m (30 h) → I-131 (8 d).

Table A4-01.1. Comparison of equilibria

Feature	Secular	Transient	No equilibrium
Half-lives	$T_p \gg T_d (>100\times)$	$T_p > T_d (\sim 10\text{--}50\times)$	$T_d > T_p$
Daughter at equilibrium	= parent	> parent (B.R. = 1) by $T_p/(T_p - T_d)$	—
Decays with	Parent $T_{1/2}$	Parent $T_{1/2}$	Own $T_{1/2}$
Example	Ge-68/Ga-68, Sr-82/Rb-82, Ra-226/Rn-222	Mo-99/Tc-99m	Te-131m/I-131

Relevance in nuclear medicine practice

- **Generators:** the long-lived parent bound on a column continuously **regrows the short-lived daughter**, which is eluted on site (CSP Table 5-3: Zn-62/Cu-62, Ge-68/Ga-68, Sr-82/Rb-82, Y-87/Sr-87m, Mo-99/Tc-99m, Sn-113/In-113m).
- **Mo-99/Tc-99m generator:**
 - After an elution, Tc-99m regrows to a **maximum about 24 h later**. Usable amounts are available **3–6 h after elution**.
 - Real **elution efficiency is 80%–90%** (it varies $\pm 10\%$). The residual Tc-99m "jump-starts" regrowth: eluting every 24 h gives about **77% of the parent activity**, with $t_{\max}$ shortened to about **21 h**.
 - Generators are used for about **1 week**, then discarded as Mo-99 decays.
 - Keeping records of actual vs predicted yields identifies **low-yield generators**.
- **Secular-equilibrium pairs** (Ge-68/Ga-68, Sr-82/Rb-82): the daughter activity equals the parent activity after about **5 daughter half-lives**, while the parent activity barely changes.
- **Sealed QC sources:** a Ge-68 source is in **secular equilibrium with its positron-emitting daughter Ga-68**, giving a long-lived 511-keV reference (dose-calibrator and well-counter checks).
- **Radionuclidic purity:** the Mo-99/Tc-99m ratio rises with time after elution because Mo-99 decays more slowly. Long-lived contaminants dominate a mixed decay curve and can be found by **curve stripping**.

Pearls

- Secular: $A_d = A_p$ after $\sim 5 T_d$; ratio > 100 (Ge-68/Ga-68, Sr-82/Rb-82).
- Transient: $A_d/A_p = T_p/(T_p - T_d)$; Mo/Tc maximum at **~23 h**, ratio ~ 0.96 (B.R. 0.876).
- No equilibrium when $T_d > T_p$ (Te-131m → I-131).
- Generator yield in practice is 80%–90% elution efficiency; usable Tc-99m 3–6 h after elution.

Sources

- CSP 4e, ch. 4 "Decay of Radioactivity", SF (mixed samples, curve stripping), p. 39; SG "Parent-Daughter Decay": G.1 "Bateman Equations", G.2 "Secular Equilibrium", G.3 "Transient Equilibrium", G.4 "No Equilibrium", pp. 39–42, Eq. 4-25 to 4-28; Fig. 4-7, p. 40.
- CSP 4e, ch. 5 "Radionuclide and Radiopharmaceutical Production", SC "Radionuclide Generators", pp. 51–52, Table 5-3, Eq. 5-13, Fig. 5-7.
- SAHA 7e, ch. 2 "Radioactive Decay", §2.3 "Successive Decay Equations", pp. 23–26, Eq. 2.9–2.14; Fig. 2.9, p. 25 (second book: half-life ratio criteria and Cs-137/Ba-137m, Sn-113/In-113m examples).
- SAHA 7e, ch. 5 "Radionuclide Generators", §5.2.1, p. 86 (rising Mo/Tc ratio after elution).
- IAEA 2014, ch. 10 "Non-Imaging Detectors and Counters", Table 10.2 (Ge-68 sealed sources in secular equilibrium with Ga-68), p. 308 (second book: QC-source application).

[4x+] A5-01 • 10 marks

Interaction of radiation with matter

- › Describe interactions of radiation with matter and its application in Nuclear Medicine. — Dec 2020 • Paper I • Q7
- › a) What are the kinds of radiation interactions with matter? [5] b) What is the significance of understanding such interactions? [5] — Jun 2022 • Paper I • Q2a–b
- › Discuss the various interaction of radiation with matter along with diagrams. [10] — Dec 2022 • Paper I • Q2
- › Discuss the non-particulate radiation interactions with matter. [10] — Dec 2023 • Paper I • Q1
- › Discuss the various types of interactions of radiation with matter and briefly describe its applications in diagnostic and therapeutic nuclear medicine. [5+5] — Jun 2024 • Paper I • Q1
- › Discuss the interaction of electromagnetic radiation with matter. [10] — Dec 2024 • Paper I • Q1

Asked in: Dec 2020 Paper I Q7 • Jun 2022 Paper I Q2a–b • Dec 2022 Paper I Q2 • Dec 2023 Paper I Q1 • Jun 2024 Paper I Q1 • Dec 2024 Paper I Q1

Kinds of radiation and how they lose energy

- Radiations from radioactive decay are of two kinds: **charged particles** (α , β^- , β^+ , electrons) and **electromagnetic radiation (photons)**: γ rays, X-rays, annihilation radiation and bremsstrahlung.
- Both transfer energy mainly by **ionisation and excitation** of atoms; most energy ends as heat. These processes underlie **radiation detection** and **radiation dosimetry**.
- Charged particles are **directly ionising**. Photons are **secondary (indirectly) ionising**: they set electrons in motion, and these electrons do the ionising.

A. Charged-particle interactions

- **Ionisation**: a close encounter strips an orbital electron. An energetic secondary electron (**δ ray**) ionises further.
- **Excitation**: a less close encounter raises an electron to an excited state; energy is lost as vibrations or IR/visible/UV emission.
- **Bremsstrahlung**: deflection by the **nuclear field** decelerates the particle, and the energy appears as a photon (radiation loss). It increases with **particle energy and Z**.
- **Collisional vs radiation losses**: in the nuclear-medicine energy range, **collisional losses dominate** (P-32 β in water: 99.6% collisional).
- **Tracks**: α particles leave **short, straight, densely ionised** tracks (microns). Electrons follow **tortuous**, longer paths (fractions of a cm) with large-angle deflections.
- **LET**: electrons 10 keV–10 MeV in soft tissue **0.2–2 keV/ μ m**; α particles **≈ 100 keV/ μ m**. Ionisation density rises near the end of the track (**Bragg peak**, marked for heavy particles).
- **Cerenkov effect**: a particle faster than light in the medium emits bluish light; <1% of electron energy.
- **Ranges**: Am-241 α (5.49 MeV) ≈ 4.2 cm in air and ≈ 54 μ m in tissue. β particles: extrapolated range in water F-18 0.23 cm, P-32 0.785 cm, Rb-82 1.65 cm.

B. Photon (electromagnetic) interactions

- Photons interact as **collisions** with an atom, nucleus or electron. Of **nine possible interactions, four matter** in nuclear medicine.

Table A5-01.1. The four photon interactions

Interaction	What happens	Products	Dependence / dominance
Photoelectric effect	Atom absorbs the whole photon; photoelectron ejected with $E_{pe} = E_0 - K_B$	Photoelectron; characteristic X-rays / Auger electrons	$\tau \propto Z^3/E^3$; K-edges (I 33.2 keV, Pb 88.0 keV); dominates in high Z at low E
Compton scattering	Photon "collides" with a loosely bound outer electron, loses part of its energy and is deflected by θ	Scattered photon + recoil electron	Nearly independent of Z and E; dominates in tissue (Z < 20) over most of the NM range
Pair production	In a nuclear field, photon converts into $e^- + e^+$; needs ≥ 1.022 MeV	Electron–positron pair $\rightarrow$ two 0.511-MeV annihilation photons	$\kappa \propto Z \log E$; dominates at high E in high Z
Coherent (Rayleigh) scattering	Photon scattered by the atom as a whole, essentially no energy loss	Scattered photon	Only at <<50 keV ; little energy transfer

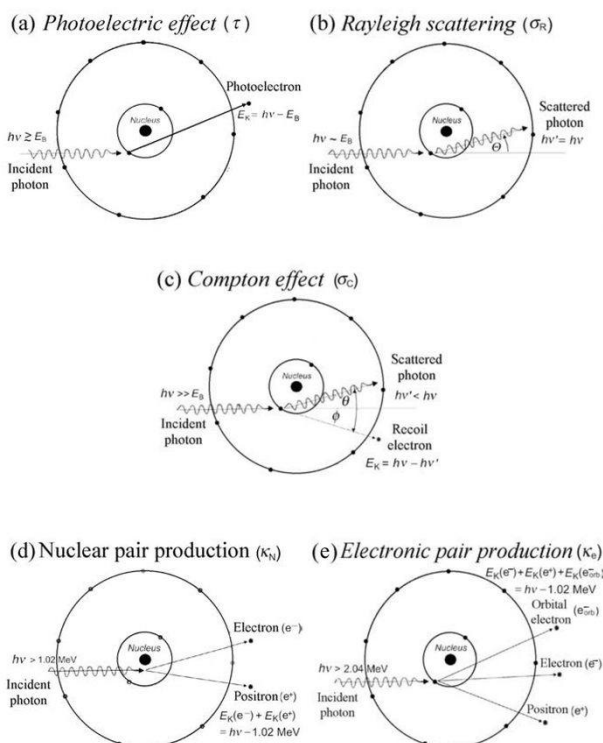
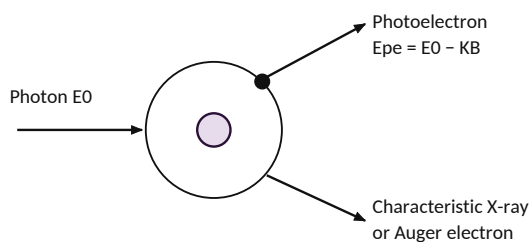


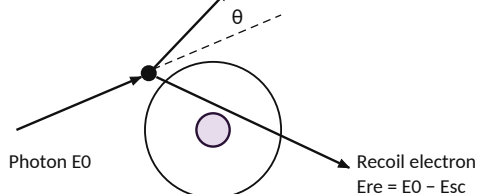
FIG. 1.9. Schematic diagrams of the most important modes of photon interaction with atoms of an absorber: (a) photoelectric effect; (b) Rayleigh scattering; (c) Compton effect; (d) nuclear pair production; and (e) electronic pair production (triplet production).

Fig. 1.9. IAEA 2014, p. 45.

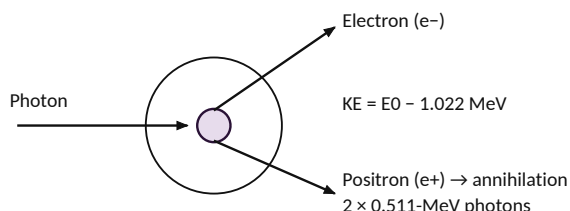
Photoelectric effect



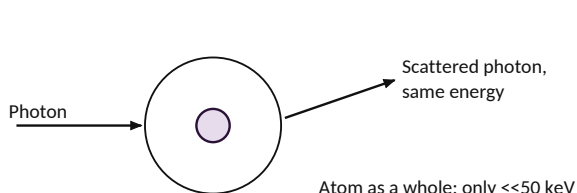
Compton scattering



Pair production ($E_0 > 1.022$ MeV)



Coherent (Rayleigh) scattering



Schematic (exam diagram): the four photon interactions of importance in nuclear medicine. Based on CSP 4e, Figs. 6-11, 6-12 and 6-14, pp. 74–77, and IAEA 2014, Fig. 1.9, p. 45; text pp. 74–77.

- **Compton energy–angle relation:** $E_{sc} = E_0 / [1 + (E_0/0.511)(1 - \cos \theta)]$. At 180° , Tc-99m 140-keV photons scatter to **91 keV** (recoil electron 49 keV); 511-keV photons scatter to 170 keV.
- The **energy change is small at low energies**, which limits rejection of scattered photons by energy discrimination.
- **Energy deposition:** a photon undergoes a **sequence** of interactions; the high-energy electrons released finally deposit the energy and cause detector signals and radiobiological effects.
- **Attenuation:** $\mu_m = \tau + \sigma + \kappa$. Narrow-beam transmission $I(x) = I(0)e^{-\mu x}$; photons have **no definite range**. HVT = $0.693/\mu$.

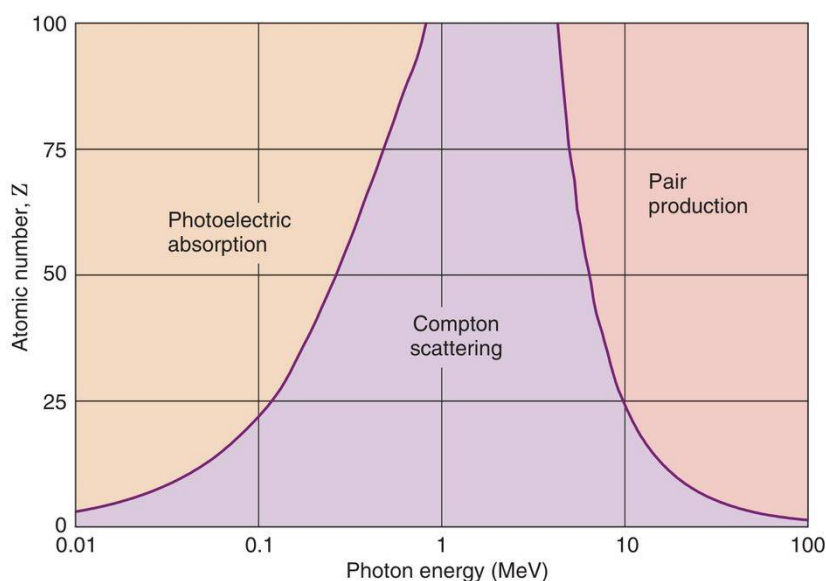


FIGURE 6-18 Predominating (most probable) interaction versus photon energy for absorbers of different atomic numbers. Curves were generated using values obtained from reference 2.

Figure 6-18. CSP 4e, p. 81.

Significance and applications in diagnostic nuclear medicine

- **Detection:** in NaI(Tl), photoelectric events give the **photopeak**; Compton events in the crystal give the Compton continuum and edge. Escaping annihilation photons give **escape peaks** when $E > 1.022$ MeV.
- **Scatter in the patient:** Compton photons degrade images and are rejected with a pulse-height window, imperfectly because the energy loss is small.
- **Attenuation in the body:** 140-keV photons are transmitted only **22%** through 10 cm of tissue (HVT 4.6 cm, narrow beam).

- **Collimators and shielding** use high-Z lead, where photoelectric absorption is strong. **Broad-beam buildup** increases transmission ($B = 1.35$ for 511 keV in 1 cm Pb).
- **Mo-99 breakthrough**: 3 mm lead is several TVTs for 140 keV but only about 1 HVT for the 700- to 800-keV γ rays of Mo-99 (beam hardening).
- **Positron range** (F-18 average 0.064 cm in water) sets a limit on PET resolution. Annihilation photons are the PET signal.
- **Beta shielding**: low-Z plastic first, then lead, to minimise bremsstrahlung.

Significance in therapeutic nuclear medicine

- **Short-range particles deposit dose locally**: β particles travel only millimetres in tissue (P-32 maximum 7.85 mm), so energy stays near the source.
- **α particles**: densely ionising ($LET \approx 100 \text{ keV}/\mu\text{m}$) with a range of tens of μm . They are harmless externally but **very potent internally**.
- **Auger electrons**: a cascade of very low-energy electrons with very short range, but ionisation densities comparable to an α track.
- **Dosimetry**: photon interactions in tissue transfer energy to electrons, so photon LET equals that of electrons ($0.2\text{--}2 \text{ keV}/\mu\text{m}$).

Pearls

- Photoelectric $\propto Z^3/E^3$; Compton $\approx$ independent of Z; pair production $\geq 1.022 \text{ MeV}$, $\propto Z$.
- **Compton dominates in soft tissue** at NM energies; photoelectric dominates in lead and NaI at low energies.
- Photons: exponential attenuation, no range. Particles: definite range.
- α : short, straight, dense tracks; β : tortuous, longer; LET 100 vs $0.2\text{--}2 \text{ keV}/\mu\text{m}$.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §A "Interactions of Charged Particles with Matter" (A.1–A.5), pp. 63–70; §B "Charged-Particle Ranges", pp. 70–73, Table 6-1; §C "Passage of High-Energy Photons Through Matter", pp. 74–78, Table 6-2, Table 6-3; §D "Attenuation of Photon Beams", pp. 78–85, Fig. 6-18, p. 81, Table 6-4, Examples 6-6 and 6-8.
- CSP 4e, ch. 10 "Pulse-Height Spectrometry", §A-B.2, pp. 142, 144.
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.1.4, p. 4; §1.6.4–1.6.11, pp. 35, 37, 45, 48; Fig. 1.9, p. 45 (second book: the five-mode schematic figure and the Auger-electron cascade, which CSP lacks).

[4x+] A5-02 • 5 marks

Bremsstrahlung

- › Define following: Bremsstrahlung Radiation. — Jun 2020 • Paper I • Q9b
- › Describe Bremsstrahlung radiation and factors affecting its production. — Dec 2020 • Paper I • Q2b
- › Bremsstrahlung radiation. [5] — Dec 2022 • Paper I • Q5a
- › Bremsstrahlung. [4] — Jun 2025 • Paper I • Q3a

Asked in: Jun 2020 Paper I Q9b • Dec 2020 Paper I Q2b • Dec 2022 Paper I Q5a • Jun 2025 Paper I Q3a

Definition

- **Bremsstrahlung** ("braking radiation"): electromagnetic radiation produced when a charged particle penetrates the electron cloud, is **deflected by the electric field of a nucleus**, and is rapidly decelerated. The energy lost appears as a photon.

Mechanism and spectrum

- The photon energy ranges from **nearly zero** (slight deflection) up to the **full kinetic energy** of the particle (particle virtually stopped). The spectrum is continuous.
- Most photons lie at the **low-energy** end, e.g. the spectrum from Sr-90/Y-90 β particles ($E_{\beta\text{max}} 2.27 \text{ MeV}$) in aluminium.
- Energy lost this way is a **radiation loss**. Ionisation and excitation are **collisional losses**, and collisional losses dominate in the nuclear-medicine energy range.

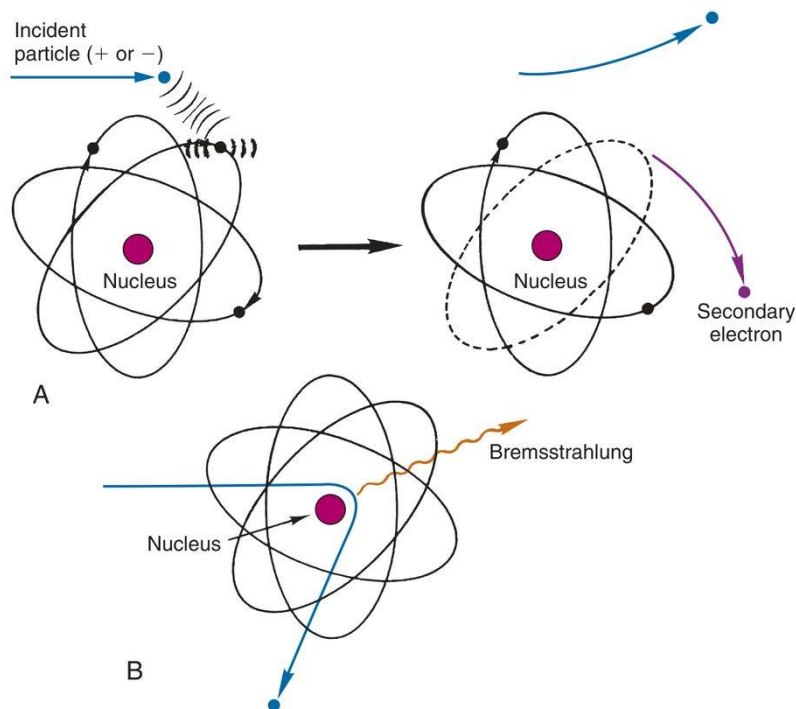


FIGURE 6-1 Interactions of charged particles with atoms. *A*, Interaction with an orbital electron resulting in ionization. Less-close encounters may result in atomic excitation without ionization. *B*, Interaction with a nucleus, resulting in bremsstrahlung production. [Repulsion by orbital electron (*A*) and attraction toward nucleus (*B*) indicates incident particles are negatively charged in the examples shown.]

Figure 6-1. CSP 4e, p. 64.

Factors affecting production

- **Atomic number of the absorber (Z):** radiation loss rises with Z .
- **Particle energy:** radiation loss rises with $E_{\beta\max}$.

$$\% \text{ radiation loss} \approx (Z \times E_{\beta\max} / 3000) \times 100 \text{ (accurate to about } \pm 30\%)$$
- For a mixture of elements use an **effective Z** (weighted by fraction by weight $\times Z^2$).
- **Particle mass: heavy particles** (α , protons) undergo few bremsstrahlung-producing collisions. Light **electrons/ β particles** are the main producers.

Worked example — P-32 β particles ($E_{\beta\max}$ 1.7 MeV), book values

- Water (Z_{eff} 7.9): $(7.9 \times 1.7/3000) \times 100 = \mathbf{0.4\%}$ radiation loss; 99.6% collisional.
- Lead ($Z = 82$): $(82 \times 1.7/3000) \times 100 = \mathbf{4.6\%}$ radiation loss; 95.4% collisional.

Practical significance

- **Shielding β emitters** (e.g. hundreds of MBq of P-32): use a **low- Z primary shield (plastic)** to stop β particles with minimal bremsstrahlung, then **lead outside** to absorb the bremsstrahlung.
- **Counting β emitters:** they can be counted through their bremsstrahlung, but counting rate per Bq is low because production efficiency is low.

Pearls

- Bremsstrahlung $\propto Z \times E$: never shield P-32 or Y-90 with lead alone.
- Continuous spectrum, maximum = particle energy, mostly low-energy photons.
- Collisional losses dominate below a few MeV (99.6% in water for P-32).

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §A.1 "Interactions of charged particles with matter" and §A.2 "Collisional Versus Radiation Losses", pp. 64–66, Eq. 6-1, 6-2, Example 6-1; Fig. 6-1, p. 64.
- CSP 4e, ch. 12 "Counting Systems", §A.10 "Applications" (well counter), p. 182.

Linear energy transfer (LET) & Bragg peak

- › Define the following: Linear Energy Transfer. — Dec 2020 • Paper I • Q9d
- › Linear energy transfer. [2] — Jun 2023 • Paper I • Q7c
- › Linear energy transfer (LET). [5] — Dec 2024 • Paper I • Q2b
- › Bragg peak in alpha radiation. [5] — Dec 2024 • Paper I • Q5a

Asked in: Dec 2020 Paper I Q9d • Jun 2023 Paper I Q7c • Dec 2024 Paper I Q2b • Dec 2024 Paper I Q5a

Linear energy transfer (LET)

- **Definition:** the energy lost by a charged particle that is **deposited locally** along its track, per unit track length. Symbol **L**, usually in **keV/μm**.
- It differs from the **linear stopping power** S_l (total energy loss rate, $\Delta E/\Delta x$ in MeV/cm) only in that LET **excludes radiation (bremsstrahlung) losses**, which deposit energy away from the track. In the NM energy range the two are practically identical.
- ICRU definition (IAEA): **dE/dl**, average energy locally imparted per distance travelled.
- **Specific ionisation (SI):** ion pairs per unit track length; $LET/SI = W$, energy per ion pair (33.7 eV in air). So $SI \propto LET$.

Table A5-03.1. Typical LET values

Radiation	LET (keV/μm)
Co-60 γ rays	0.2
1-MeV electrons	0.25
Electrons 10 keV–10 MeV in soft tissue	0.2–2
250-kVp X-rays	2.0
10-MeV protons	4.7
α particles	≈100 (2.5-MeV α: 166)

Factors affecting LET

- **Charge and velocity:** α particles carry two charges and move slowly (4-MeV α ≈ 10% of c vs 1-MeV electron ≈ 90% of c), so they ionise about **100 times more densely** than electrons of the same energy.
- **Particle energy:** LET rises as the particle **slows down**.
- **Medium density:** energy-loss rate rises linearly with density.
- Photons have the LET of the electrons they release (0.2–2 keV/μm).

Significance

- High-LET radiation (α, neutrons) causes more irreversible chromosome damage, which is the basis of the radiation weighting factor (w_R 20 for α).
- **Average LET correlates poorly with biological effect** because LET varies along the track; the directly measured **RBE** is preferred.

Bragg peak in alpha radiation

- Because specific ionisation **increases as a particle slows down**, ionisation density rises sharply near the **end of its range**. This is the **Bragg ionisation peak**, especially pronounced for heavy particles such as α.
- For α particles in air, specific ionisation rises towards the end of the track to a sharp peak just before the particle stops, then falls to zero (CSP Fig. 6-7).
- In electrons, a similar rise occurs only below ~1 keV and carries little of the total energy.
- **Use:** in proton therapy, the beam energy is chosen so that the Bragg peak falls **within the tumour**.

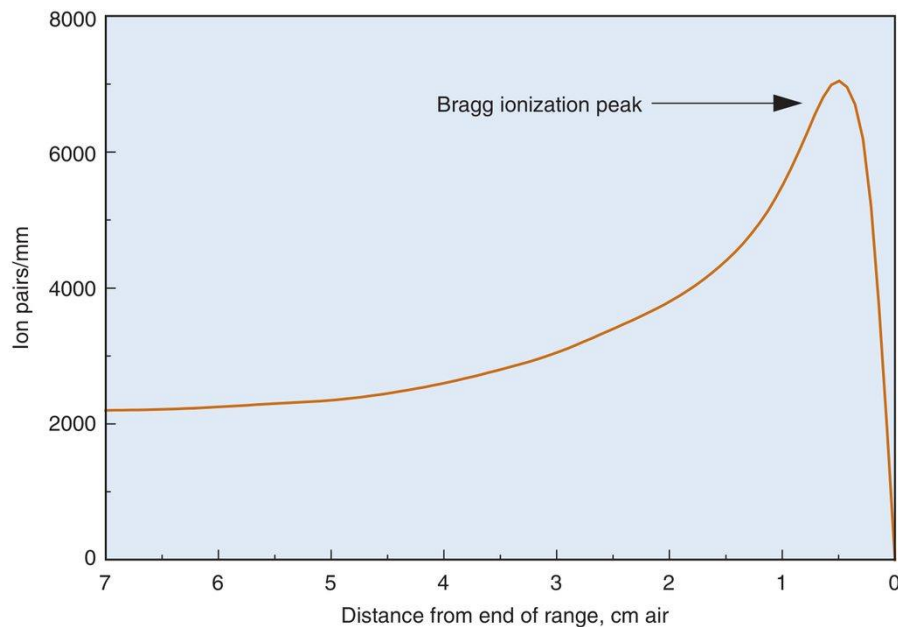


FIGURE 6-7 Specific ionization versus distance traveled for α particles in air. (Adapted from Mladjenovic M: Radioisotope and Radiation Physics. New York, 1973, Academic Press, p 111.)

Figure 6-7. CSP 4e, p. 69.

Pearls

- LET = locally deposited energy per μm ($\text{keV}/\mu\text{m}$); stopping power includes bremsstrahlung.
- Electrons $0.2\text{--}2 \text{ keV}/\mu\text{m}$ (low LET); $\alpha \approx 100 \text{ keV}/\mu\text{m}$ (high LET).
- Bragg peak = ionisation maximum at the end of a heavy-particle track.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §A.3 "Charged-Particle Tracks" and §A.4 "Deposition of Energy Along a Charged-Particle Track", pp. 66–69, Eq. 6-3 to 6-5; Fig. 6-7, p. 69; §C.6, p. 78.
- IAEA 2014, ch. 2 "Basic Radiobiology", §2.6.3 "Dose deposition characteristics: linear energy transfer", pp. 57–58, Table 2.2 (second book: ICRU definition and LET values for Co-60, X-rays and protons, which CSP lacks); ch. 3, §3.2.3.1, p. 78.

[3×] A5-04 • 5 marks

Cerenkov radiation & Cerenkov luminescence imaging

- › Define following: Cerenkov Radiation. — Jun 2020 • Paper I • Q9c
- › Cerenkov luminescence imaging. [5] — Dec 2023 • Paper I • Q10b
- › Cerenkov radiation and its clinical applications in nuclear medicine. [5] — Dec 2025 • Paper I • Q8b

Asked in: Jun 2020 Paper I Q9c • Dec 2023 Paper I Q10b • Dec 2025 Paper I Q8b

Cerenkov radiation: definition

- Light emitted when a **charged particle travels through a medium faster than the speed of light in that medium** ($c' = c/n$).
- The particle creates an **electromagnetic "shock wave"**, like the sonic boom of a supersonic aircraft. It appears as a burst of **visible, typically bluish** light.
- Example: a 1-MeV β particle in water moves at $\approx 0.8c$, while light in water ($n = 1.33$) travels at $\approx 0.75c$.

Conditions and properties

- **Threshold:** electrons of a few hundred keV. In water, β particles above **263 keV** produce Cerenkov light. Heavy particles (α , protons) need several thousand MeV, so they practically never produce it.
- It accounts for **<1%** of electron energy in the NM energy range.
- The light is emitted in a **directional cone** and is weighted toward the **blue end** of the visible spectrum.
- It produces the **bluish glow** in the water around an operating reactor core.

Applications in nuclear medicine (from the books)

- **Cerenkov counting:** high-energy β emitters are assayed in a liquid-scintillation counter **without scintillator**, by detecting the Cerenkov light with the PM tubes.
 - Mainly for **P-32** ($E_{\beta\max}$ 1710 keV), with counting efficiency **>50%**.
 - There is **no chemical quenching** (a physical process), but **colour quenching** must be corrected. Calibration must allow for the light cone and spectrum.

NOT COVERED IN SOURCE

- **Cerenkov luminescence imaging (CLI)** and other clinical Cerenkov applications: searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "Cerenkov", "Cherenkov", "luminescence", "optical imaging". Checked CSP ch. 6 and ch. 12 and REQ ch. 5 "Molecular Imaging". CLI is not described.
- Related material: REQ lists **optical imaging** in general as high sensitivity and high resolution, but with **limited depth of detection** and limited clinical use.
- Where the terms occur: 'Cerenkov' only as the Cerenkov effect (CSP 4e ch. 6 §A.5, pp. 68–70) and Cerenkov counting in liquid-scintillation systems (CSP ch. 12, p. 188); 'Cherenkov' once, in a REQ figure legend (e-book PDF p. 41).

Pearls

- Cerenkov = particle speed $> c/n$ of the medium; bluish, directional light.
- Threshold in water for β : 263 keV; α practically never.
- Cerenkov counting of P-32 in an LSC without scintillator: >50% efficiency, no chemical quench.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §A.5 "The Cerenkov Effect", pp. 68–70.
- CSP 4e, ch. 12 "Counting Systems", §C.7 "Cerenkov Counting", p. 188.
- REQ 5e, ch. 5 "Molecular Imaging" (comparison of imaging modalities), e-book PDF p. 231 (second book: related optical-imaging material only).

[3×] A5-05 • 5 marks

Pair production, Rayleigh scatter & photodisintegration

- > Write about Pair production and Rayleigh Scatter. [5] — Jun 2023 • Paper I • Q5a
- > Pair production and photo disintegration. [4] — Jun 2025 • Paper I • Q10a
- > Pair production and its clinical applications in nuclear medicine. [5] — Dec 2025 • Paper I • Q8a

Asked in: Jun 2023 Paper I Q5a • Jun 2025 Paper I Q10a • Dec 2025 Paper I Q8a

Pair production

- A photon interacts with the **electric field of a charged particle**, usually a nucleus and occasionally an electron. The photon disappears and an **electron–positron pair** is created.
- **Threshold:** rest mass of each particle is 0.511 MeV, so $E_0 \geq 1.022 \text{ MeV}$.

$$E_{e^+} + E_{e^-} = E_0 - 1.022 \text{ MeV}$$

- Kinetic energy is shared randomly, usually **20%–80%**. Both particles lose energy by ionisation and excitation.
- The positron, once stopped, **annihilates** with an electron, giving **two 0.511-MeV photons** emitted in opposite directions. Usually only the kinetic energy is deposited locally.
- **Nuclear pair production** (threshold 1.022 MeV) contributes >90%. **Electronic (triplet) production** in an orbital electron's field needs **2.044 MeV**.
- **Dependence:** zero below threshold, then rises with energy. $\kappa \propto Z \log E$ (mass coefficient $\propto Z$). Dominates at **high energies in high-Z absorbers**.

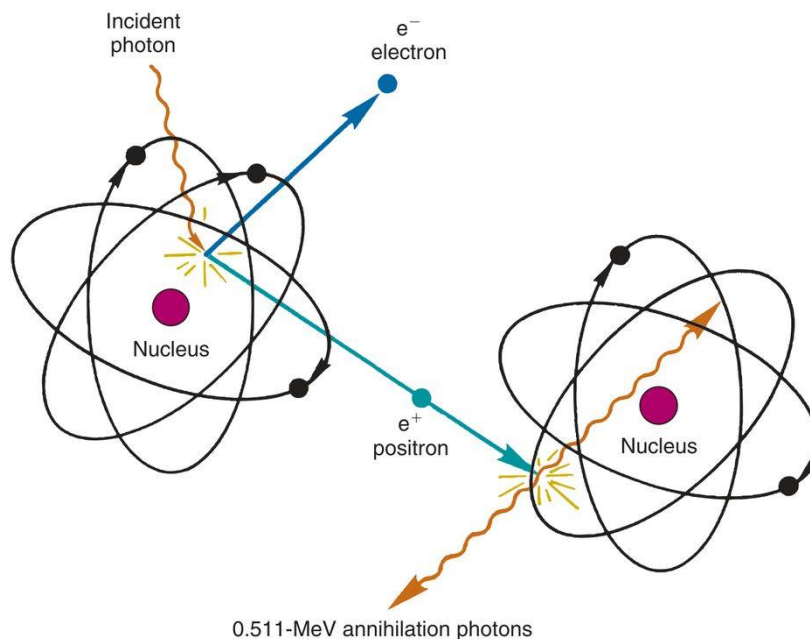


FIGURE 6-14 Schematic representation of pair production. Energy of incident photon is converted into an electron and a positron (total 1.022-MeV mass-energy equivalent) plus their kinetic energy. The positron eventually undergoes mutual annihilation with a different electron, producing two 0.511-MeV annihilation photons.

Figure 6-14. CSP 4e, p. 77.

Rayleigh (coherent) scattering

- The photon interacts with the **atom as a whole** (all tightly bound electrons). The atom's large mass absorbs almost no recoil energy, so the photon is **deflected with essentially no energy loss**, through a small angle.
- Important only at **low energies** (<50 keV). Atomic coefficient $\propto Z^2/(h\nu)^2$; mass coefficient $\propto Z/(h\nu)^2$.
- It **removes photons from a beam** (relevant to precise transmission measurements and CT, a few % of μ/ρ in tissue) but transfers **no energy**, so it is irrelevant to dosimetry.

Photodisintegration (photonuclear reaction)

- A **direct photon–nucleus interaction** in which the photon is **absorbed completely** by the nucleus. It is listed among photon interactions with absorber nuclei.

NOT COVERED IN SOURCE

- Photodisintegration thresholds, the particles emitted and reaction examples: searched all five books, full text and index pages, for "photodisintegration", "photo-disintegration", "photonuclear", " (γ, n) ". Checked CSP ch. 6 and IAEA ch. 1. Only the one-line statement above (IAEA §1.6.4) exists.

Relevance to nuclear medicine

- Most NM photon energies are **below 1.022 MeV**, so pair production is minor in clinical imaging.
- In detector spectra of emitters above 1.022 MeV it produces **single-escape** ($E_\gamma - 511$ keV) and **double-escape** ($E_\gamma - 1.022$ MeV) peaks.
- **Annihilation photons**, the PET signal, come from positron decay; positrons from pair production annihilate the same way.

Pearls

- Pair production: $E_0 \geq 1.022$ MeV (triplet ≥ 2.044 MeV); ends in two 511-keV photons.
- Rayleigh: no energy loss, low energies only, no dose.
- Escape peaks in spectra are the signature of pair production in the detector.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §C.1 "Photon Interaction Mechanisms", p. 74; §C.4 "Pair Production" and §C.5 "Coherent (Rayleigh) Scattering", pp. 76–77, Eq. 6-15; Fig. 6-14, p. 77; §D.1, p. 79.
- CSP 4e, ch. 10 "Pulse-Height Spectrometry", §B.2 "The Actual Spectrum", pp. 144–145.
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.6.4 (photonuclear reaction), pp. 35, 37; §1.6.6 "Rayleigh (coherent) scattering", p. 39; §1.6.8 "Pair production", pp. 44–46 (second book: triplet production, Z dependence of Rayleigh scattering and photonuclear reactions, which CSP

[2×] A5-06 • 5 marks

Photoelectric & Compton effect

> Compton effect. [2] — Jun 2023 • Paper I • Q7a

> Photoelectric and Compton Effect. [2.5+2.5] — Jun 2024 • Paper I • Q9a

Asked in: Jun 2023 Paper I Q7a • Jun 2024 Paper I Q9a

Photoelectric effect

- An **atomic absorption** process: the atom absorbs the **entire photon energy**, the photon disappears and an orbital electron (**photoelectron**) is ejected.

$$E_{pe} = E_0 - K_B \quad (K_B = \text{binding energy of the shell})$$

- Needs $E_0 > \text{binding energy}$. Ejection is most likely from the **innermost possible shell**: K-shell is 4–7 times more likely than L-shell.
- The vacancy causes **characteristic X-rays or Auger electrons**.
- $\tau \propto Z^3/E^3$: dominant in **heavy elements at low energy**. Abrupt rise ($\times 5$ – 6) at **K absorption edges**: iodine 33.2 keV, lead 88.0 keV.
- In **soft tissue** binding energies are only a few keV, so nearly all the photon energy goes to the photoelectron and is deposited **near the interaction site**. In iodine or lead, binding energy (20–100 keV) takes a significant share.

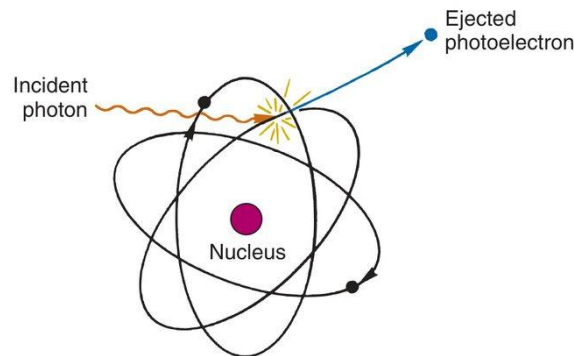


FIGURE 6-11 Schematic representation of the photoelectric effect. The incident photon transfers its energy to a photoelectron and disappears.

Figure 6-11. CSP 4e, p. 74.

Compton scattering

- A "collision" between a photon and a **loosely bound outer-shell electron** (effectively free). The photon is **deflected by θ** and loses part of its energy to the **recoil electron**.

$$E_{sc} = E_0 / [1 + (E_0/0.511)(1 - \cos \theta)] ; E_{re} = E_0 - E_{sc}$$

- Energy transfer ranges from ~ 0 (grazing, $\theta \approx 0^\circ$) to a maximum at **180° backscatter**. The scattered photon never reaches zero energy; $E_{sc, \min}$ approaches **255.5 keV** at high energies.
- Small energy change at low energy** (Tc-99m 140 keV $\rightarrow$ 91 keV at 180°) makes scatter rejection by energy windows difficult.
- Angular distribution**: at 10–100 keV, scatter is forward and backward with a minimum at 90° ; well above 0.5 MeV, scatter is increasingly **forward**.
- σ nearly independent of Z and E**. Compton is dominant for intermediate Z and E, and in **body tissues ($Z < 20$)** over most of the NM range.

Table A5-06.1. Photoelectric vs Compton

Feature	Photoelectric	Compton
Electron involved	Tightly bound (inner shell)	Loosely bound (outer shell)
Photon after event	Absorbed (disappears)	Scattered with lower energy
Products	Photoelectron + X-rays/Auger	Scattered photon + recoil electron
Z, E dependence	$\propto Z^3/E^3$	$\approx$ independent of Z; slow fall with E
NM relevance	Photopeak in NaI(Tl); lead shielding and collimators	Scatter in the patient; Compton continuum and edge in spectra

Pearls

- Photoelectric: all-or-none absorption; **K-edges**; $\propto Z^3/E^3$.
- Compton: partial energy loss; dominates in soft tissue; 180° backscatter gives the maximum transfer.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §C.2 "The Photoelectric Effect" and §C.3 "Compton Scattering", pp. 74–76, Eq. 6-10 to 6-14, Table 6-2; Fig. 6-11, p. 74; §D.1 (τ , σ dependence and dominance), pp. 79, 81.

[1×] A5-07 • 5 marks

Types of Neutron interactions with matter. [5]

Asked in: Jun 2023 Paper I Q6b

Neutrons: why they interact differently

- Neutrons carry **no electric charge**, so they are neither attracted nor repelled by nuclei and are unaffected by the Coulomb barrier. Even **thermal neutrons (0.025 eV)** can enter a nucleus and cause a reaction.
- They are **indirectly ionising**: an uncharged particle first releases a charged particle, which then ionises the medium.
- **Fast neutrons** from fission (up to ~10 MeV) are slowed to thermal energies by a **moderator** (water, heavy water, graphite). Thermal neutrons are the more efficient initiators of fission.

Types of neutron interactions

Table A5-07.1. Neutron interactions with matter

Type	What happens	Example
Elastic scattering	Products identical to reactants; total kinetic energy and momentum conserved	—
Inelastic scattering	Products identical, but part of the energy leaves the target as internal excitation energy E^*	—
Radiative capture (n,γ)	Target captures a thermal neutron, forms an excited compound nucleus, which emits a prompt γ ray . Product is an isotope of the same element (low specific activity, not carrier-free)	$^{98}\text{Mo}(n,\gamma)^{99}\text{Mo}$; $^{59}\text{Co}(n,\gamma)^{60}\text{Co}$; $^{176}\text{Lu}(n,\gamma)^{177}\text{Lu}$
Charged-particle emission (n,p), (n,α)	Neutron captured, proton or α particle emitted; product is a different element , so (n,p) products can be carrier-free	$^{32}\text{S}(n,p)^{32}\text{P}$; $^{14}\text{N}(n,p)^{14}\text{C}$; $^{35}\text{Cl}(n,\alpha)^{32}\text{P}$
Fission (n,f)	A fissile nucleus (U-235) absorbs a neutron, splits into two fragments and releases 2–3 neutrons (chain reaction)	$^{235}\text{U}(n,f)^{99}\text{Mo}$, I-131, Xe-133

Products of neutron activation

- Adding neutrons puts the product **above the line of stability**, so it usually decays by **β[−] emission**.
- (n,γ) and (n,p) both produce **prompt** emissions at the moment of capture; the radioactive product then decays with its own half-life.
- Targets placed at different reactor positions see **neutrons of different energies**, which selects between thermal and fast reactions.

Reaction cross-section and yield

- **Thermal-neutron reactions** have **large cross-sections** and high reactor fluxes ($\sim 10^{14}$ n/cm²·s), so yields are high.

- **Fast-neutron reactions** have cross-sections of **millibarns** and lower fluxes, so yields are lower, but some nuclides (e.g. P-32) must be made this way.
- Only 1 in 10^6 to 10^9 target nuclei are activated, so (n,γ) products have **low specific activity**.

Applications

- **Reactor radionuclide production** (Mo-99, I-131, Lu-177, Y-90, P-32).
- **Neutron activation analysis** of trace elements (n,γ).

Pearls

- No charge → reacts even at 0.025 eV; indirectly ionising.
- (n,γ) = same element, low specific activity; (n,p)/(n,α) = new element, carrier-free.
- A moderator slows fission neutrons to thermal energies; control rods (Cd, B) absorb neutrons.

Sources

- CSP 4e, ch. 5 "Radionuclide and Radiopharmaceutical Production", §A.1 "Reactor Principles", p. 43; §A.3 "Neutron Activation", pp. 45–46.
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.1.4, p. 4; §1.3.4 "Two-particle collisions and nuclear reactions", p. 14; ch. 4 "Radionuclide Production", §4.2.1–4.2.2, pp. 128–130, Table 4.1 (second book: elastic/inelastic scattering, (n,α) and fast-neutron reactions, which CSP does not cover).
- SAHA 7e, ch. 4 "Production of Radionuclides", §4.2.2 "Neutron Capture or (n, γ) Reaction", pp. 61–62 (second book: neutron activation analysis).

A6 Attenuation & shielding — HVL, TVL, specific gamma-ray constant

[4x+] A6-01 • 10 marks

HVL & TVL

- › Define the following: Tenth Value Layer. — Dec 2020 • Paper I • Q9c
- › What is the importance of Half value layer (HVL) and Tenth value layer (TVL)? Enumerate three applications of each in day to day Nuclear Medicine practice. [4+6] — Jun 2022 • Paper I • Q4
- › Half value and tenth value layer. [5] — Dec 2023 • Paper II • Q2a
- › Derive HVL and TVL equations. [5] — Jun 2024 • Paper IV • Q8a
- › HVL and TVL in radiation shielding. [5] — Dec 2024 • Paper I • Q6b
- › Define HVL and TVL along with their relations. Discuss clinical applications of HVL and TVL. [5+5] — Dec 2025 • Paper I • Q7

Asked in: Dec 2020 Paper I Q9c • Jun 2022 Paper I Q4 • Dec 2023 Paper II Q2a • Jun 2024 Paper IV Q8a • Dec 2024 Paper I Q6b • Dec 2025 Paper I Q7

Definitions

- **Half-value layer (HVL) / half-value thickness (HVT):** the thickness of absorber that **reduces the recorded (narrow-beam) intensity to one half**.
- **Tenth-value layer (TVL) / tenth-value thickness (TVT):** the thickness that **reduces the intensity to one tenth**. It is useful when relatively **thick shields** are needed.
- **Mean free path (MFP):** the average distance a photon travels before interacting; it reduces the intensity to 1/e (36.8%).

Derivation

- For a thin absorber, the fractional decrease in intensity is proportional to thickness: $dI/I = -\mu dx$, where μ is the **linear attenuation coefficient** (cm^{-1}).
- Integrating from 0 to x for a monoenergetic narrow beam:

$$I(x) = I(0) e^{-\mu x}$$

- **HVL:** put $I(\text{HVL}) = 0.5 I(0)$, so $e^{-\mu \cdot \text{HVL}} = 1/2$, giving $\mu \cdot \text{HVL} = \ln 2$:

$$\text{HVL} = x_{1/2} = \ln 2 / \mu \approx 0.693 / \mu$$

- **TVL:** put $I(\text{TVL}) = 0.1 I(0)$, so $e^{-\mu \cdot \text{TVL}} = 1/10$, giving $\mu \cdot \text{TVL} = \ln 10$:

$$\text{TVL} = x_{1/10} = \ln 10 / \mu \approx 2.303 / \mu$$

- **MFP** = $1/\mu$.

Relations between them

$$\text{TVL} = (\ln 10 / \ln 2) \times \text{HVL} \approx 3.32 \times \text{HVL} ; \text{HVL} = 0.301 \times \text{TVL} ; \text{MFP} = \text{HVL} / \ln 2 \approx 1.44 \times \text{HVL}$$

- The relation mirrors radioactive decay: μ replaces λ , thickness replaces time, and HVL is the analogue of half-life.
- **n HVLs** transmit $(1/2)^n$; **n TVLs** transmit $(1/10)^n$.

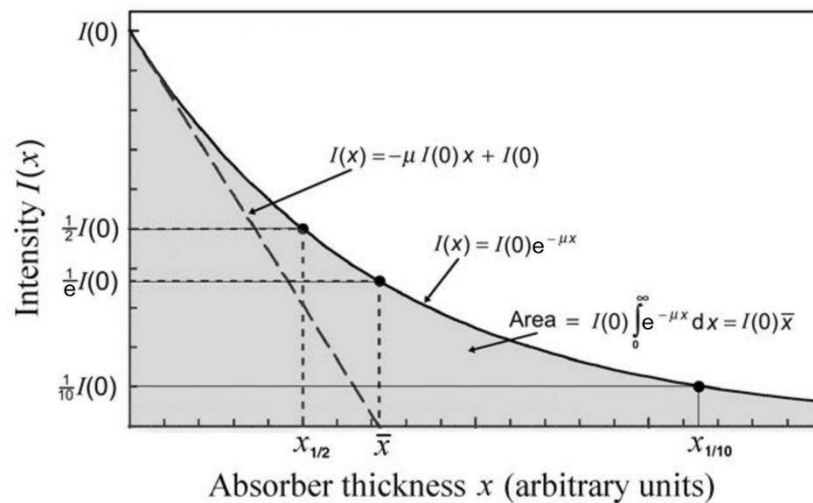


FIG. 1.4. Intensity $I(x)$ against absorber thickness x for a monoenergetic photon beam. Half-value layer $x_{1/2}$, mean free path $\bar{x}$ and tenth-value layer $x_{1/10}$ are also illustrated. The area under the exponential attenuation curve from $x = 0$ to $x = \infty$ is equal to the product $I(0)\bar{x}$ where $I(0)$ is the initial intensity of the monoenergetic photon beam. The slope of the tangent to the attenuation curve at $x = 0$ is equal to $\mu I(0)$ and this tangent crosses the abscissa (x) axis at $x = \bar{x}$.

Fig. 1.4. IAEA 2014, p. 33.

Table A6-01.1. HVT in water and TVT in lead (narrow beam)

Radionuclide	Photon energy (keV)	HVT in water (cm)	TVT in lead (mm)
I-125	27.5	1.7	0.06
Xe-133	81	4.3	1.0
Tc-99m	140	4.6	0.9
I-131	364	6.3	7.7
Annihilation (β^+)	511	7.1	13.5
Co-60	1330	11.2	36.2

Factors that determine HVL and TVL

- **Photon energy:** higher energy, larger HVL (water HVT 1.7 cm at 27.5 keV vs 11.2 cm at 1330 keV).
- **Absorber:** μ rises linearly with **density**; $\mu_m = \mu/\rho$ (cm^2/g) removes the density effect and depends on **Z and E**. High-Z lead has a far smaller TVL than water (Tc-99m: 0.9 mm Pb).
- **Mixtures:** μ_m is the weight-fraction sum of the component values (e.g. water = 2/18 H + 16/18 O).
- **Photons have no definite range:** $I(x)$ never reaches zero, unlike charged particles, which is why shielding is specified as HVLs or TVLs.

Important caveats

- HVL and TVL are exact only for a **monoenergetic, narrow (good-geometry) beam**.
- **Broad-beam** conditions (real shielding, photons from inside the patient) add scattered photons. Transmission becomes $T = B e^{-\mu x}$, with **buildup factor** $B > 1$, so more shielding is needed than the narrow-beam figure suggests.
- **Polyenergetic emitters** (Ga-67, I-131) cannot be described by a single HVL: transmission is a sum of exponentials, and the beam **hardens** with depth. Use measured **broad-beam transmission tables** instead.
- Measured broad-beam transmission through lead (IAEA Table 9.7): Tc-99m **0.105 at 1 mm** and 0.00835 at 2 mm; I-131 0.116 at 10 mm; 511 keV 0.249 at 10 mm. Higher-energy emitters need far more lead.

Worked example — Transmission of 140-keV photons through 10 cm of tissue (CSP Example 6-6)

- HVT (water, 140 keV) = 4.6 cm, so $\mu = 0.693/4.6 = \mathbf{0.151\text{ cm}^{-1}}$.
- $I(10)/I(0) = e^{-0.151 \times 10} = e^{-1.51} = \mathbf{0.221\text{ (22\%)}}$.

Worked example — Shielding 511-keV photons with 1 cm lead (CSP Examples 6-7, 6-8)

- TVT of 511 keV in lead = 13.5 mm, so HVT = $1.35\text{ cm}/3.32 = \mathbf{0.41\text{ cm}}$ (book rounds to 0.4 cm).
- 1 cm = $1/0.4 = \mathbf{2.5\text{ HVTs}}$, so narrow-beam transmission = $(1/2)^{2.5} = \mathbf{0.18\text{ (18\%)}}$.
- Broad beam: $\mu x = 0.693/0.4 \times 1 = 1.73$, so $B \approx 1.35$ and $T \approx 1.35 \times 0.18 = \mathbf{0.24\text{ (24\%)}}$.

Worked example — Lead needed to cut I-131 dose rate 1000-fold (narrow beam, from Table 6-4)

- $1000 = 10^3$, so **3 TVLs** are needed.
- TVT of 364-keV photons in lead = 7.7 mm, so thickness = $3 \times 7.7 = \mathbf{23.1\text{ mm}}$ ($\approx 10\text{ HVLs}$, since $3 \times 3.32 = 9.96$).
- In real broad-beam geometry buildup raises transmission, so somewhat more lead is required (compare IAEA Table 9.7: 20 mm Pb transmits 0.0132 of I-131).

Importance and applications in day-to-day nuclear medicine

- TVL simplifies shielding arithmetic: **each TVL is a factor of 10**, so required attenuation factors (10^2 , 10^3) translate directly into a number of TVLs.

Table A6-01.2. Applications

Quantity	Uses
HVL	Attenuation in the patient: Tc-99m HVT in tissue is 4.6 cm, so only 22% of 140-keV photons pass through 10 cm of tissue (narrow beam).
	Quick transmission estimates: number of HVLs gives the transmission factor through a shield, like a decay factor.
	Mo-99 breakthrough check: 3 mm lead is about 1 HVT for the 700- to 800-keV Mo-99 γ rays but several TVTs for 140 keV, so Mo-99 can be measured through a lead pot (beam hardening).
TVL	Design of thick shields: radiopharmacy walls, enclosures, body shields at the dispensing station, and vial and syringe shields (lead or tungsten for γ emitters).
	Generator shielding: >100 GBq Mo-99 generators with 740-keV photons need several cm of lead (a lead "garage").
	PET (511 keV) shielding: TVT 13.5 mm lead, so positron-emitter shielding is set by the annihilation photons, not the positrons.

Pearls

- $\text{HVL} = 0.693/\mu$; $\text{TVL} = 2.303/\mu$; **TVL $\approx 3.32\text{ HVL}$** ; $\text{MFP} = 1/\mu \approx 1.44\text{ HVL}$.
- Valid for narrow, monoenergetic beams only; broad-beam buildup increases transmission.
- Tc-99m: HVT 4.6 cm water; TVT 0.9 mm lead. 511 keV: TVT 13.5 mm lead.

Sources

- CSP 4e, ch. 6 "Interaction of Radiation with Matter", §D.1–D.4 "Attenuation of Photon Beams", pp. 78–85, Eq. 6-16, 6-22 to 6-27, Table 6-4, Examples 6-6 to 6-8.
- IAEA 2014, ch. 1 "Basic Physics for Nuclear Medicine", §1.6.1–1.6.2 "Characteristic absorber thicknesses", pp. 31–33, Eq. 1.44–1.52; Fig. 1.4, p. 33 (second book: formal derivation and the HVL–TVL–MFP relation).
- IAEA 2014, ch. 9 "Physics in the Radiopharmacy", §9.8.1–9.8.2 "Shielding for Radionuclides", pp. 274–275, 278–279 (second book: practical shielding applications and broad-beam transmission tables).

Specific gamma-ray constant

- > Specific gamma ray constant. — Jun 2020 • Paper I • Q7b
- > Specific gamma ray constant. [5] — Dec 2022 • Paper I • Q7a
- > Specific gamma ray constant. [3] — Jun 2023 • Paper I • Q7b
- > Specific gamma ray constant and its utility in nuclear medicine. [5] — Dec 2024 • Paper I • Q2a

Asked in: Jun 2020 Paper I Q7b • Dec 2022 Paper I Q7a • Jun 2023 Paper I Q7b • Dec 2024 Paper I Q2a

Definition

- The **specific gamma-ray constant** (now expressed as the **air kerma rate constant, Γ**) is a radionuclide-specific value. It gives the **air kerma rate in mGy/h at 1 m from an unshielded 1-GBq point source**.
- Units: **mGy·m²/GBq·h**.
- Older form, the **exposure rate constant**: exposure in **R/h at 1 cm from 1 mCi** (R·cm²/mCi·h). 1 R·cm²/mCi·h = 27.027 μ Gy·m²/GBq·h.

How it is derived

- Calculated from the **number of γ and X-rays per disintegration**, their **energies**, and the **absorption coefficient of air** at those energies:

$$\Gamma = 199 \sum N_i E_i \mu_i \quad (N_i \text{ abundance, } E_i \text{ in MeV, } \mu_i \text{ mass absorption coefficient of air})$$

- Only photons above a cut-off (typically **20 keV**: Γ_{20}) are included, because lower-energy photons are stopped by syringe or vial walls and pose a negligible external hazard.

Use: dose rate from a source

$$K \text{ (mGy/h)} = \Gamma \times A \text{ (GBq)} / d^2 \text{ (m}^2\text{)}$$

- The d^2 term is the **inverse-square law** (photons are emitted isotropically).
- Valid only at distances **large compared with the source size**; it fails on contact (e.g. hand doses from syringes), where measured values are used.
- Exposure rate (R/h) $\approx$ air kerma rate (mGy/h) $\times$ 0.115.

Table A6-02.1. Air kerma rate constants (Γ , mGy·m²/GBq·h)

Radionuclide	Γ	Radionuclide	Γ
Tc-99m	0.0141	F-18	0.1351
I-123	0.0361	Ga-68	0.1290
I-131	0.0522	Ga-67	0.0195
In-111	0.0831	Tl-201	0.0102
Mo-99/Tc-99m (equilibrium)	0.0336	Cs-137/Ba-137	0.0821

Worked example — Air kerma rate from a 1-GBq Tc-99m syringe (CSP Example 23-1)

- At 10 cm: $K = 0.0141 \times 1 / (0.1)^2 = \mathbf{1.41 \text{ mGy/h}}$.
- At 300 cm: $K = 0.0141 \times 1 / (3)^2 = 1.57 \times 10^{-3} \text{ mGy/h} = \mathbf{1.57 \mu\text{Gy/h}}$.
- Moving from 10 cm to 3 m cuts the rate 900-fold.

Utility in nuclear medicine

- Estimating **staff dose rates** around patients, syringes, vials and waste, which guides **time, distance and shielding** under ALARA.
- **Shielding and facility design**: positron emitters have Γ about **10 times** that of Tc-99m (F-18 0.1351 vs 0.0141).
- **Survey-meter calibration**: expected dose rate $D = \Gamma A e^{-\lambda \Delta t} / d^2$ from a reference source (Co-57, Ge-68, Cs-137); readings should agree within **10%**.
- Equivalent and effective dose rates can be estimated from air kerma rates with weighting factors, but depend on geometry.



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Radionuclide Therapy

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SESSIONS

162

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6

YEARS

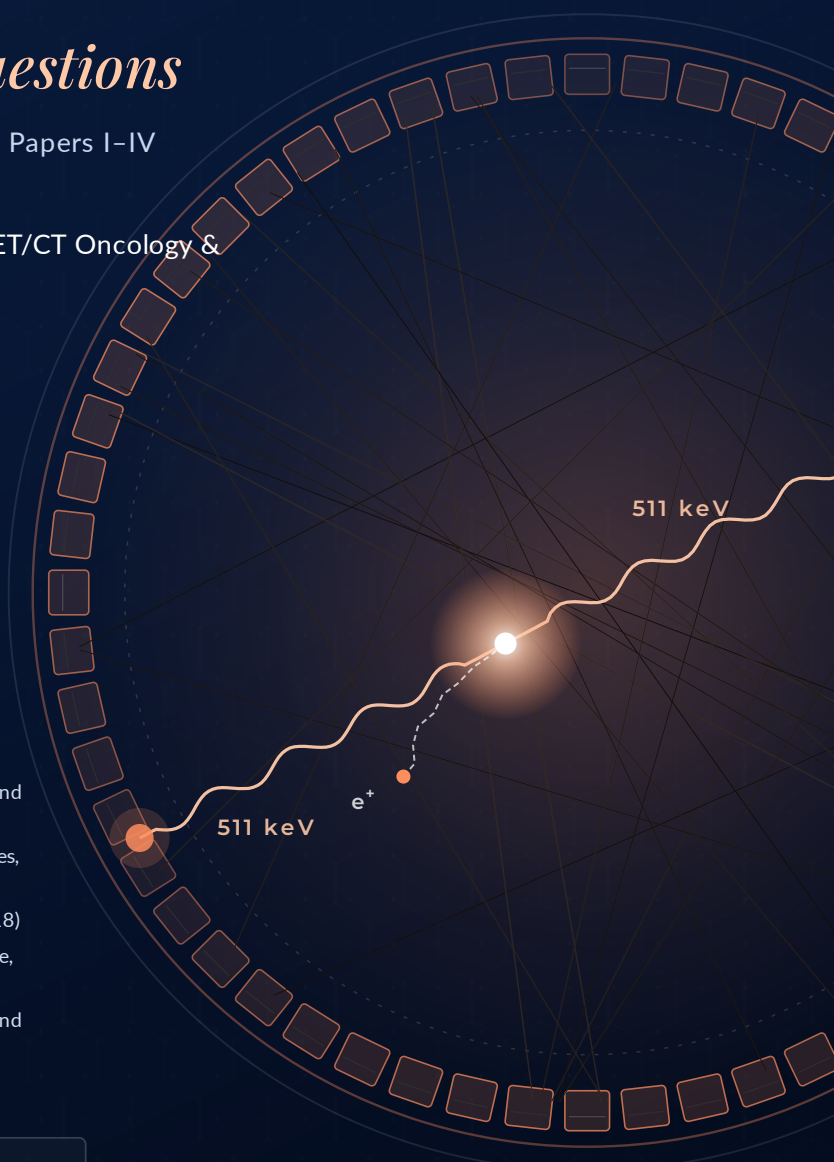
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REVIEWED BY

Dr Gaurav Sharma & Dr Aditi Pal

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Clinical Nuclear Medicine, PET/CT Oncology & Radionuclide Therapy

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REVIEWED BY

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How to use these notes

- **One answer, many questions.** Repeated and near-repeated questions are answered once. Each answer heading lists every version with its paper tag; the badge (1×, 2×, 3×, 4×+) shows how often it was asked.
- **Red box: NOT COVERED IN SOURCE.** The point was searched in all five textbooks (full text and index) and is not there. The box names the searches.
- **Amber box: current guideline.** An official guideline or consensus document (body, document, year), placed after the main answer.
- **Figures.** Book figures carry their own figure number and page. Schematics are original simplified exam diagrams and are labelled "Schematic (exam diagram)".
- **Sources.** MET 7e = Mettler & Guiberteau, Essentials of Nuclear Medicine and Molecular Imaging, 7th ed (2019); REQ 5e = Nuclear Medicine and Molecular Imaging: The Requisites, 5th ed (2021; e-book pages); SAHA 7e = Fundamentals of Nuclear Pharmacy, 7th ed (2018); CSP 4e = Physics in Nuclear Medicine, 4th ed (2012); IAEA 2014 = Nuclear Medicine Physics: A Handbook for Teachers and Students.

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H1-01	Insulinoma & functional pancreatic NETs — imaging (incl. exendin)	6×	210
H1-02	NET imaging — SPECT & PET tracers	4×	212
H1-03	NETPET score	3×	215
H1-04	WHO classification & grading of NETs	3×	217
I1-01	Immunotherapy response — pseudo/hyper-progression, iRECIST, iPERCIST	6×	222
I1-02	Response evaluation criteria — RECIST, PERCIST, EORTC	4×	223
I2-01	Brain tumours — PET/SPECT tracers & recurrence	6×	228
I4-01	Breast cancer — staging & PET/CT (NCCN, LABC)	3×	242
I5-01	Prostate cancer PET/SPECT tracers (PSMA, choline, fluciclovine)	7×	249
I6-01	Lymphoma — PET/CT staging, Deauville & response	3×	260
I6-02	Multiple myeloma — PET/CT	3×	262
I9-01	PET/CT-guided biopsy & interventions	5×	274
F4-01	Paediatric DTC — management (incl. pulmonary metastases)	3×	281
F5-01	RAI-refractory DTC — definition, diagnosis & management	6×	286
F5-02	TKIs in thyroid cancer (incl. trials)	4×	289
F5-03	TENIS — evaluation & management	3×	292
H2-01	PRRT — principles, protocol, indications & adverse effects	6×	298

Answer	Theme	Times asked	Page
H2-02	Nephroprotection in PRRT	3×	301
J1-01	Alpha vs beta vs Auger emitters for therapy	4×	303
J2-01	Alpha emitters & targeted alpha therapy	7×	309
J2-02	Actinium-225 — decay scheme, production & nanogenerator	5×	311
J3-01	PSMA RLT trials — VISION, TheraP & ongoing trials	5×	314
J4-01	Bone pain palliation radiopharmaceuticals	3×	325
J5-01	TACE vs TARE / SIRT	3×	330
J5-02	TARE / SIRT — indications, procedure & dosimetry	3×	331
J6-01	I-131 MIBG therapy — neuroblastoma, protocol & complications	3×	334
I10-01	FAPI imaging & theranostics	8×	340
I10-02	F-18 FDOPA PET — clinical applications	5×	342
I10-03	CXCR4 / Pentixafor imaging	4×	343
I10-04	Hypoxia imaging	4×	344
I10-05	Angiogenesis imaging	3×	346

L1 Dementia

[4x+] L1-01 • 6 marks

Amyloid & tau PET imaging

- › Tau imaging in dementia. — Jun 2020 • Paper II • Q6b
 - › Amyloid imaging. — Dec 2020 • Paper IV • Q5a
 - › Amyloid vs. Tau Imaging. [5] — Jun 2021 • Paper IV • Q10a
 - › Amyloid and Tau PET/CT imaging in Alzheimer's disease. [5] — Dec 2021 • Paper IV • Q3a
 - › Beta amyloid imaging agents used in PET and their clinical applications. [6] — Jun 2025 • Paper II • Q6a
- Asked in: Jun 2020 Paper II Q6b • Dec 2020 Paper IV Q5a • Jun 2021 Paper IV Q10a • Dec 2021 Paper IV Q3a • Jun 2025 Paper II Q6a

The two target proteins

- Alzheimer disease (AD) has two abnormal proteins:
 - extracellular "senile" plaques of **β -amyloid ($A\beta$)**;
 - intracellular **neurofibrillary tangles (NFTs)**, made of hyperphosphorylated **tau**.
- **Amyloid cascade hypothesis**: $A\beta$ deposition incites neuroinflammation, NFT formation, vascular damage and synaptic loss, which lead to neuronal death.
- **$A\beta$ deposits decades before symptoms** and plateaus years before they peak. Its volume and distribution do not reflect the stage or severity of disease.
- **Tau spreads with functional decline**: anteromesial temporal lobe and hippocampus, then lateral temporal and temporoparietal cortex, then the posterior cingulate cortex (PCC) and superior posterior parietal lobe.
 - Unlike amyloid, **the amount of tau correlates with disease severity**.
 - Tau also defines other "**tauopathies**": behavioural-variant FTL, corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP).

β -amyloid PET agents

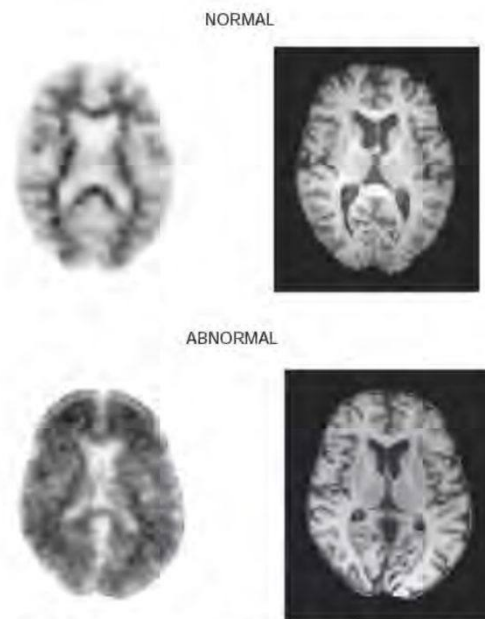
- Thioflavin-T derivatives that cross the blood–brain barrier and bind $A\beta$.
- **C-11 PIB** (Pittsburgh compound B) was the first and most studied: it binds in >90% of AD, but its 20-min half-life limits clinical use.
- **F-18 FDDNP** is less specific: it also binds NFTs and other proteins.
- Uptake of the approved F-18 agents (e.g. F-18 flutemetamol) matches AD pathology at post-mortem in **>90%** of patients.

Table L1-01.1. FDA-approved F-18 amyloid agents

Agent (trade name)	Activity	Uptake (waiting) period	Note
F-18 florbetapir (Amyvid)	10 mCi (370 MBq)	30–60 min	—
F-18 florbetaben (Neuraceq)	8 mCi (300 MBq)	45–120 min	—
F-18 flutemetamol (Vizamyl)	5 mCi (185 MBq)	90 min	Post-mortem concordance >90%

- **No fasting**, glucose control or change in insulin is needed. 3-D acquisition: one bed position for 10 min.

Reading an amyloid scan



• **Fig. 3.19** Cerebral Amyloid Plaque Positron Emission Tomography (PET) Imaging. PET images were obtained with ^{18}F -florbetapir. A normal scan in a healthy control demonstrates nonspecific low white-matter binding with preservation of gray-white matter discrimination. The abnormal scan in a patient with Alzheimer disease demonstrates extensive amyloid neuritic plaque in the cerebral cortex. (Modified from Cattell L, Platsch G, Pfeiffer R, et al. Classification of amyloid status using machine learning with histograms of oriented 3D gradients. *NeuroImage Clin* 2015;12:990–1003. Available from: <http://dx.doi.org/10.1016/j.nicl.2015.09.003>.)

Fig. 3.19. MET 7e, p. 77.

- **Negative:** little or no cortical binding, with nonspecific white-matter activity. Grey-white contrast is crisp (a "white-matter display lacking a grey-matter cortex"), and the interhemispheric fissure is clearly seen.
- **Positive:** cortical activity **blurs the grey-white boundary** and may erase the interhemispheric fissure; it is usually symmetric.
 - In AD it involves the lateral temporal and parietal lobes, frontal lobe, **precuneus and PCC**, sometimes the caudate.
 - Sensory, motor and visual cortex and cerebellum stay negative.
- **Cerebellar cortex** is the normal reference for visual reading.
- **Read rule:** positive = cortical grey-matter uptake in **at least two brain regions** ("moderate to severe amyloid plaques"); negative = "no to sparse" amyloid.
- Semiquantitative methods help in atrophy or equivocal scans. Readers need additional training.
- Amyloid PET is **96% sensitive and 100% specific** for amyloid plaque, with a high negative predictive value.

Clinical applications of amyloid PET

- **Confirms AD** and separates it from **frontotemporal dementia (FTD)** and Parkinson disease, which are amyloid-negative. Dementia with Lewy bodies (DLB) may be positive: amyloid is present in **50%–70% of DLB**.
- Usually positive in **MCI due to early AD**, so it helps predict which MCI cases will progress.
- **Appropriate use** (Box 3.2, SNMMI–Alzheimer's Association 2013):
 - persistent or progressive unexplained MCI;
 - possible AD with an unusual presentation or course;
 - progressive dementia with atypically early onset (<65 years).
- **Inappropriate use:**
 - asymptomatic patients;
 - age ≥ 65 already meeting classic AD criteria;
 - family history or ApoE- $\epsilon 4$ alone;
 - in lieu of genetic testing;
 - to assess severity;
 - nonmedical (legal, insurance) use.
- **Impact:** diagnosis changes in 23%–30% and management in 60%.

- **Limitations:**

- cortical uptake in **30%–50% or more of cognitively normal elderly**;
- amyloid burden does not track severity;
- binding occurs in other neurodegenerative disorders, so a positive scan is **not pathognomonic**;
- a negative scan lowers the likelihood of AD but does not exclude it.

Tau PET

- In MET (2019), tau-specific tracers were **not yet clinically available**; they may help differentiate tau pathologies.
- REQ (2021) lists **F-18 flortaucipir (AV-1451)** for tau deposition as an experimental agent; F-18 FDDNP binds A β , tau and other proteins.
- **Rationale:** tau tracks severity and spreads in step with symptoms, which amyloid does not.

Table L1-01.2. Amyloid PET versus tau PET

Feature	Amyloid PET	Tau PET
Target	Extracellular A β plaques	Intracellular NFTs (hyperphosphorylated tau)
Timing	Decades before symptoms; plateaus early	Spreads with functional decline
Relation to severity	Poor	Correlates with severity
Disease spectrum	AD; DLB (50%–70%); 30%–50% of normal elderly	AD; also bvFTLD, CBD, PSP (tauopathies)
Agents in the books	F-18 florbetapir, florbetaben, flutemetamol; C-11 PIB	F-18 flortaucipir (experimental); F-18 FDDNP (nonspecific)

Current guideline (beyond the textbook)

- **Alzheimer's Association & SNMMI · Updated Appropriate Use Criteria for Amyloid and Tau PET (Rabinovici et al., J Nucl Med 2025;66 Suppl 2:S5–S31; the "2024 update") · 2025.** The textbook predates this.
- The tau tracer **F-18 flortaucipir** received FDA approval in **2020**.
- Tau PET is rated **appropriate** in 5 scenarios:
 - MCI or dementia in patients <65 years with suspected AD pathology (score 8);
 - MCI or dementia possibly due to AD but with atypical features (7);
 - prognosis in MCI due to suspected AD (7);
 - prognosis in dementia due to suspected AD (7);
 - eligibility for an approved amyloid-targeting therapy (8).
- Amyloid and tau PET are **not routinely recommended together**.

Pearls

- Amyloid = early, plaque, poor correlation with severity; tau = tangles, follows symptoms.
- A positive amyloid scan shows **loss of grey–white contrast in ≥ 2 cortical regions**; the cerebellum is the reference.
- A negative amyloid scan has a **high negative predictive value** for AD; **FTD is amyloid-negative**.
- 30%–50% of healthy elderly are amyloid-positive: never use it as a screening test.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Alzheimer Disease: Amyloid Imaging in Dementia", pp. 73–77, Table 3.2, p. 74, Table 3.3, p. 76, Box 3.2, p. 77, Fig. 3.19, p. 77; Pearls & Pitfalls, p. 84; §"SPECT and PET Brain Imaging", p. 63.
- REQ 5e, ch. 14 "Central Nervous System", Table 14.2, e-book PDF p. 1026; §"Abnormal Proteins in Alzheimer's Disease", pp. 1042–1048; amyloid PET agents, interpretation and accuracy, Box 14.7–14.9, pp. 1076–1087 (second book: tau biology, read rule, protocol and accuracy figures that MET does not give).

Dementia — FDG patterns (AD, DLB, FTD, rapidly progressive)

- › Lewy body dementia (LBD). — Dec 2020 • Paper IV • Q5b
- › a) Lewy body dementia. [2.5] b) Fronto-temporal dementia. [2.5] c) Posterior Cingulate sign. [2.5] — Jun 2021 • Paper III • Q6a–c
- › Radiopharmaceuticals being used in dementia. [5] — Jun 2022 • Paper II • Q7b
- › Rapid onset dementia - causes and role of PET. [5] — Dec 2023 • Paper IV • Q10a
- › Role of PET/CT in Alzheimer disease, dementia with Lewy bodies and frontotemporal lobar dementia. [5+3+2] — Jun 2024 • Paper III • Q9

Asked in: Dec 2020 Paper IV Q5b • Jun 2021 Paper III Q6a–c • Jun 2022 Paper II Q7b • Dec 2023 Paper IV Q10a • Jun 2024 Paper III Q9

Radiopharmaceuticals used in dementia

Table L1-02.1. Agents for dementia imaging

Agent	Localises by	Role
F-18 FDG (PET)	Regional glucose metabolism	Pattern diagnosis of neurodegenerative dementia
Tc-99m HMPAO / Tc-99m ECD (SPECT)	Regional cerebral blood flow	Perfusion pattern; mirrors FDG with lower accuracy
F-18 florbetapir, florbetaben, flutemetamol	β-amyloid deposition	Excluding or identifying possible AD
I-123 ioflupane (DaTscan)	Presynaptic dopamine transporter	DLB versus AD
I-123 MIBG (cardiac)	Sympathetic nerve terminals	Decreased in DLB (supportive)
F-18 flortaucipir	Tau deposition	Experimental (in REQ)

Technique and normal FDG brain

- Inject FDG in a **quiet, darkened room, patient awake with eyes open**. Closed eyes lower visual-cortex uptake and can mimic the **occipital hypometabolism of DLB**.
- Sedatives, antiepileptics, neuroleptics and barbiturates alter regional metabolism.
- **Preparation:** fast 4–6 h; glucose <200 mg/dL; F-18 FDG 8 mCi (296 MBq) (range 5–12 mCi, 185–444 MBq); uptake period 35–60 min.
- **Normal pattern:** basal ganglia and thalami highest, then cortical grey matter; white matter very low.
 - The PCC, Wernicke area, frontal eye fields and posterior parietal lobes may be relatively hypermetabolic.
 - Frontal metabolism falls with normal ageing.
- FDG PET beats perfusion SPECT in detecting and classifying dementia (**accuracy >90%**). Always inspect the **anterior and posterior cingulate gyri and the precuneus**.

Alzheimer disease

- **Bilateral posterior temporal and parietal association cortex, precuneus and PCC** hypometabolism.
- **Spared:** primary sensorimotor and visual cortex, basal ganglia, thalamus, brainstem and cerebellum.
- Early disease may be **asymmetric** (about 30%); **frontal** involvement appears with advanced disease.
- FDG: sensitivity **75%–99%** and specificity **71%–93%** (REQ: up to 94% and 83%). SPECT: 65%–85% and 72%–87%.
- Not pathognomonic; also seen in Parkinson disease dementia (often with occipital reduction), vascular dementia and encephalopathies.

Posterior cingulate sign

- **Focal PCC hypometabolism** is one of the **earliest** FDG findings in AD.
- It is the most easily seen abnormality in early AD, and the **most specific finding for separating AD from FTLD**.
- PCC and temporoparietal hypometabolism also **predict conversion of MCI to AD** (accuracy 58%–100%, high negative predictive value).
- The PCC lies in the medial posterior parietal lobe above the corpus callosum (Brodmann areas 23, 29, 31). It is hard to see on a single slice, so check it in all planes.

- **Contrast:** in DLB the PCC is relatively preserved, the "**cingulate island sign**".

Dementia with Lewy bodies

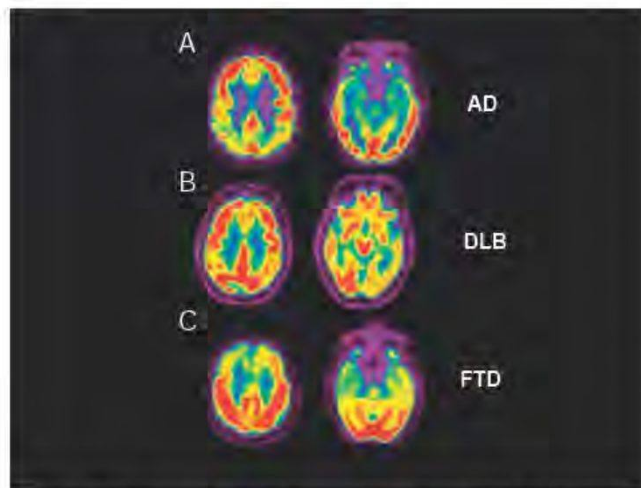
- The second most common neurodegenerative dementia (**15%–25%**). Core features: fluctuating cognition, visual hallucinations and REM sleep behaviour disorder.
- FDG and perfusion patterns resemble AD (parietal, posterior temporal and posterior cingulate), **plus occipital (especially medial) hypometabolism**, the most specific abnormality.
 - The cingulate island sign may be present.
 - Cerebellar and earlier frontal involvement can occur.
 - If the occipital cortex is spared, FDG cannot separate AD from DLB.
- **I-123 ioflupane:** decreased striatal (especially putaminal) uptake favours DLB, with sensitivity 78%–88% and specificity 90%–100%. Clinical assessment alone: 75% and 42%.
- **Cardiac I-123 MIBG** uptake is also decreased. Amyloid is present in 50%–70%.
- **Why it matters: neuroleptics are contraindicated** in DLB (irreversible parkinsonism or autonomic dysfunction).

Frontotemporal dementia (FTLD; Pick disease)

- Presents earlier; **personality and behaviour change before memory loss**. FTLD causes almost half of dementias before 60–65 years.
- FDG: **frontal and anterior temporal hypometabolism with anterior cingulate involvement**; sensorimotor cortex spared.
- Three patterns: (1) bilateral frontal + anterior temporal + anterior cingulate; (2) frontal with temporal sparing; (3) temporal-predominant, often asymmetric (semantic variant).
- Crossed cerebellar diaschisis may occur. **Amyloid PET is negative**.
- Acetylcholinesterase inhibitors should be **avoided** (they can worsen behaviour, no benefit).

Table L1-02.2. FDG/perfusion patterns of the main dementias

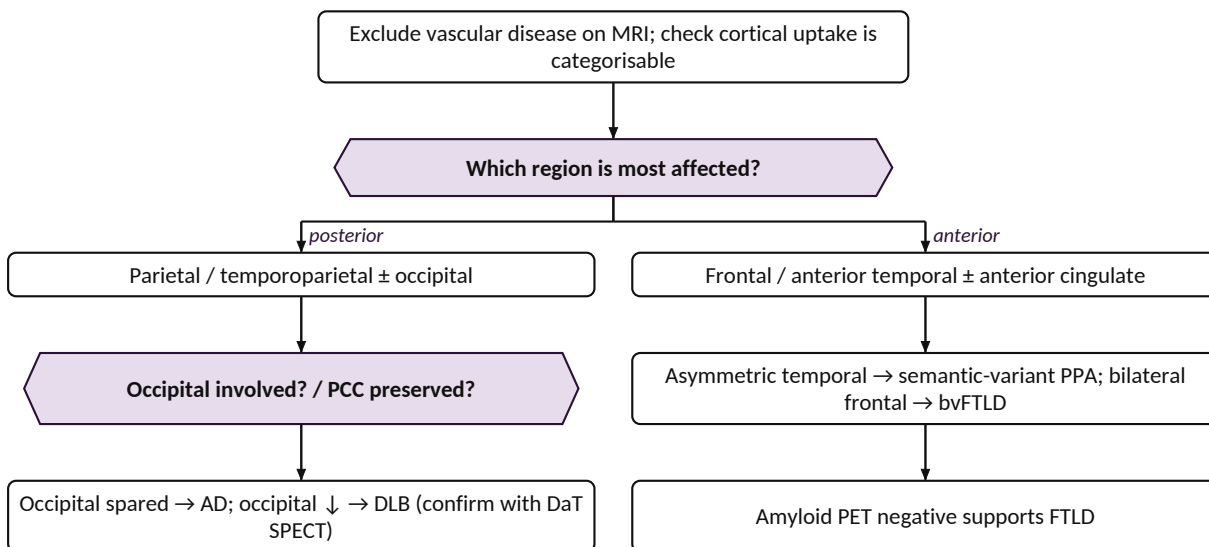
Disease	Decreased	Preserved
AD	Bilateral posterior parietotemporal, posterior cingulate, precuneus; frontal later	Sensorimotor and visual cortex, basal ganglia, thalamus, cerebellum, anterior cingulate
DLB	As AD (posterior parietotemporal, posterior cingulate) plus medial occipital ; caudate; striatum on DaT	Sensorimotor cortex, cerebellum; anterior cingulate and frontal lobe (variable)
FTD	Frontal, anterior temporal, anterior cingulate	Sensorimotor, occipital, posterior parietotemporal (early)
Multi-infarct	Scattered, asymmetric cortical and deep defects	Variable
Huntington	Caudate and lentiform nuclei; frontal and temporal	Occipital cortex



• **Fig. 3.20** Typical Positron Emission Tomography ^{18}F -Fluorodeoxyglucose Uptake Patterns in Major Neurodegenerative Dementias. (A) Alzheimer dementia (AD) with characteristic parietotemporal hypometabolism. (B) Dementia with Lewy bodies (DLB) also demonstrates parietotemporal hypometabolism; however, additional occipital hypometabolism is often present, a finding not characteristic for AD. (C) Frontotemporal dementia (FTD) with classic frontal and temporal hypometabolism. (Modified from Nasrallah I, Dubroff J. An overview of PET neuroimaging. *Semin Nucl Med.* 2013;43(6):449–461. Available from: <http://dx.doi.org/10.1053/j.semnucmed.2013.06.003>.)

Fig. 3.20. MET 7e, p. 78.

Flowchart L1-02.1. Systematic FDG reading in neurodegenerative dementia (REQ Fig. 14.12 approach)



Rapid-onset dementia: causes and role of PET

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "rapid onset dementia", "rapidly progressive", "Creutzfeldt", "prion", "encephalitis", "limbic". Checked MET ch. 3 and REQ ch. 14.
- REQ lists Creutzfeldt–Jakob (prion) disease only among neurodegenerative disorders with abnormal protein deposition. No imaging pattern or role of PET for rapid-onset dementia is given.
- Related book material: multi-infarct (vascular) dementia, with scattered asymmetric defects, can be separated from AD on perfusion SPECT or FDG PET.

Current guideline (beyond the textbook)

- EANM • Procedure guidelines for brain PET imaging using [18F]FDG, version 3 (Guedj et al., Eur J Nucl Med Mol Imaging 2022;49:632–651) • 2021/2022. The textbook predates this.
- Encephalitis (autoimmune, infectious and postinfectious) is a listed indication. FDG PET is especially relevant when MRI is negative or inconclusive.
- Typical autoimmune-encephalitis pattern: **global hypometabolism with striatal and limbic relative hypermetabolism** (sensitivity 80%–90%).
- Scan before steroids where possible. Whole-body PET can look for a cancer in paraneoplastic syndromes.

Pearls

- **AD = posterior** (temporoparietal, PCC, precuneus); **FTD = anterior** (frontal, anterior temporal, anterior cingulate); **DLB = AD + occipital**, PCC spared.
- All three neurodegenerative dementias **spare the sensorimotor cortex**.
- Eyes must be open during FDG uptake, or occipital "DLB" artefact results.
- AD-like FDG pattern + abnormal DaT scan = DLB.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"SPECT and PET Brain Imaging" and §"PET/CT Image Interpretation", p. 63; §"Dementia", pp. 72–78, Table 3.2, p. 74, Fig. 3.20, p. 78; Pearls & Pitfalls, pp. 83–84.
- REQ 5e, ch. 14 "Central Nervous System", Table 14.1, e-book PDF p. 1024; Box 14.2, pp. 1034–1035; Box 14.5, p. 1042; §"Alzheimer's Disease", pp. 1052–1057, Table 14.6–14.7, Fig. 14.12, pp. 1055–1063; §"Dementia With Lewy Bodies", pp. 1059–1060; §"Frontotemporal Dementia", pp. 1064, 1071–1072, Table 14.8 (second book: cingulate island sign, accuracy data, FTLD patterns and treatment risks that MET does not give).

[1×] L1-03 • 10 marks

Multimodality imaging in the evaluation and management of Alzheimer's disease. [10]

Asked in: Jun 2023 Paper IV Q3

Why imaging is multimodal in AD

- Post-mortem histology remains the gold standard. In life, the diagnosis now combines **clinical criteria with biomarkers** (NIA-AA 2011 revision).
- **Biomarkers of Aβ deposition**: positive amyloid PET or low CSF Aβ42.
- **Biomarkers of neuronal injury**: raised CSF tau (total and phosphorylated); **entorhinal or hippocampal atrophy on MRI**; **temporoparietal hypometabolism on FDG PET**.
- Certainty that dementia is due to AD:
 - **high** when Aβ is positive **and** a neuronal-injury marker is positive;
 - **intermediate** with either one;
 - **uncertain** with no positive or conflicting biomarkers.
- Imaging tests are more accurate than clinical examination alone.

Table L1-03.1. Biomarker staging of AD (REQ Table 14.4, NIA-AA 2011 with modifications)

Category	Cognition	Aβ (PET or CSF)	Neuronal injury (tau, MRI, FDG)
Preclinical stage 1	Normal	+	–
Preclinical stage 2	Normal	+	+
Preclinical stage 3	Subtle change	+	+
SNAP (suspected non-Alzheimer pathophysiology)	—	–	+
MCI	Mild; daily living preserved	+	+
AD dementia	Affects daily living	+	+

Structural imaging: MRI and CT

- **MRI** shows atrophy of the **hippocampus, entorhinal cortex and amygdala**; sensitivity 83% and specificity 85%. **CT**: 80% and 87%.

- MRI is the first step in reading a dementia PET: it **excludes or confirms significant vascular disease** and other structural causes.
- FDG changes may appear **before atrophy is seen on MRI**.
- MET: PET for AD is used together with **MR haemodynamic imaging, MR spectroscopy and volumetric techniques**. Fusion of SPECT or PET with MRI greatly helps anatomic localisation.

Functional imaging: perfusion SPECT and FDG PET

- **Perfusion SPECT** (Tc-99m HMPAO or ECD):
 - shows symmetric defects in the posterior temporal and parietal cortex, precuneus and posterior cingulate gyri, with positive predictive value **>75%–80%**;
 - asymmetric in about 30%;
 - a normal scan has a high negative predictive value.
- **FDG PET**:
 - same pattern with greater accuracy; the earliest sign is **focal posterior cingulate hypometabolism**;
 - frontal involvement appears with progression;
 - sensorimotor and visual cortex, basal ganglia, thalamus and cerebellum are spared.
- FDG is a marker of **neuronal injury**. PCC and temporoparietal hypometabolism **predict which MCI cases convert to AD** (high negative predictive value; more accurate than MRI).
- MCI: about 15% convert to AD in 2 years and more than a third in 5 years.

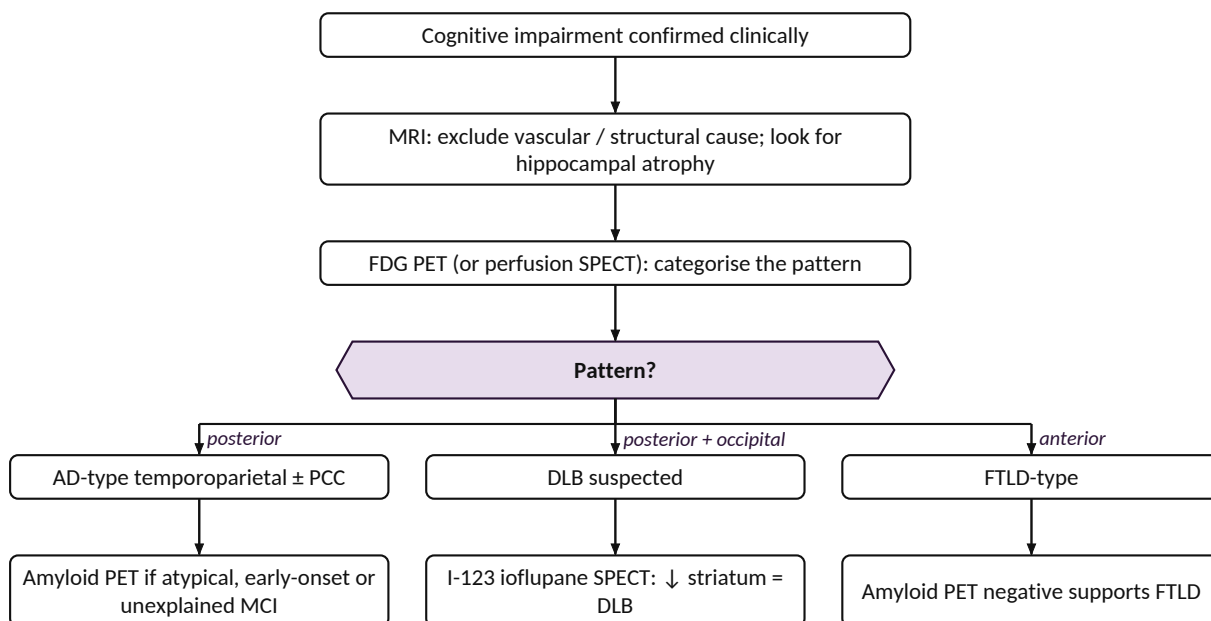
Molecular imaging: amyloid, tau and dopamine transporter

- **Amyloid PET** (F-18 florbetapir, florbetaben, flutemetamol):
 - positive = cortical grey-matter uptake in ≥ 2 regions;
 - **96% sensitive, 100% specific** for plaque, with high negative predictive value;
 - but positive in **30%–50% of healthy elderly**, so it is used per appropriate-use criteria;
 - it is the biomarker that best separates **AD (positive) from FTLT (negative)**.
- **IDEAS study** (>11,400 patients, 2019): amyloid PET changed the diagnosis from non-AD to AD in 10.5% and from AD to non-AD in 25.1%. The composite endpoint changed in 63.5% (dementia) and 60.2% (MCI).
- **Tau PET** (F-18 flortaucipir) was experimental in the books. Tau tracks severity, unlike amyloid.
- **I-123 ioflupane DaT SPECT**: when FDG shows an AD-like pattern, decreased striatal uptake points to **DLB** instead.

Table L1-03.2. What each modality contributes

Modality	Shows	Sensitivity	Specificity
MRI	Hippocampal/entorhinal atrophy; vascular disease	83%	85%
CT	Atrophy	80%	87%
Perfusion SPECT	Posterior temporoparietal hypoperfusion	79%	84%
FDG PET/CT	Temporoparietal, PCC hypometabolism	91%	85%
CSF A β	Low A β 42	76%	77%
CSF tau	Raised total/phospho-tau	78%	85%
Amyloid PET	Cortical A β plaques	96%	100% (for plaque)

Flowchart L1-03.1. Multimodality pathway in suspected AD (from the book steps)



Imaging in management

- **Correct diagnosis directs therapy:**
 - AD: acetylcholinesterase inhibitors are approved;
 - DLB: **neuroleptics are contraindicated**;
 - FTD: **avoid donepezil**.
- **Amyloid status** matters most for persistent or progressive unexplained MCI, atypical or mixed presentations, early-onset dementia, and selecting patients for **experimental anti-amyloid therapy**.
- Amyloid-lowering drugs had not yet altered cognitive decline in trials (as of the books).
- Serial FDG PET documents progression: anterior spread, frontal involvement and eventually global decline.

Current guideline (beyond the textbook)

- **Alzheimer's Association & SNMMI · Updated Appropriate Use Criteria for Amyloid and Tau PET (Rabinovici et al., J Nucl Med 2025;66 Suppl 2) · 2025.** The textbook predates this.
- The criteria cover PET to determine **eligibility for newly approved amyloid-targeting treatments** and to follow treated patients.
- Tau PET is rated appropriate for **eligibility for an approved amyloid-targeting therapy** (score 8), and for diagnosis and prognosis in suspected AD (early-onset or atypical MCI/dementia).
- Amyloid and tau PET are not routinely recommended together.

Pearls

- High-certainty AD = **Aβ biomarker + neuronal-injury biomarker** (tau, MRI atrophy or FDG).
- MRI excludes vascular disease and shows hippocampal atrophy; FDG shows the pattern; amyloid PET answers "is it AD pathology?"
- **FDG PET/CT** has the highest sensitivity of the routine tests (91%); amyloid PET is the most specific for plaque.
- An AD-like FDG pattern with occipital involvement or an abnormal DaT scan → DLB: avoid neuroleptics.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Dementia" and §"Alzheimer Disease", pp. 72–77; Fig. 3.17, p. 75.
- REQ 5e, ch. 14 "Central Nervous System", §"Abnormal Proteins in Alzheimer's Disease", pp. 1043, 1047; §"Alzheimer's Disease", pp. 1050–1057, Table 14.3–14.6; DLB, p. 1060; Table 14.8, p. 1071; amyloid PET and IDEAS trial, pp. 1078, 1086–1087 (second book: NIA-AA biomarker framework, accuracy table, MCI conversion and management data that MET does not give).

L2 Movement disorders

[4x+] L2-01 • 10 marks

Movement disorders & Parkinsonism — NM imaging

- › Role of nuclear medicine imaging in movement disorders. — Dec 2020 • Paper III • Q2
- › PET in movement disorders. [5] — Jun 2021 • Paper IV • Q5a
- › Nuclear medicine evaluation in patients with tremors. [5] — Dec 2022 • Paper IV • Q6b
- › Role of nuclear medicine in Parkinson Plus Syndromes. [5] — Jun 2023 • Paper III • Q8b
- › a) Discuss about the PET & SPECT radiopharmaceuticals used for movement disorder imaging. [4] b) Discuss their mechanism of uptake, relative advantages and disadvantages. [6] — Dec 2023 • Paper II • Q8a-b
- › a) Enumerate the various causes of movement disorders. [4] b) Discuss the role of nuclear medicine imaging in typical and atypical Parkinson's disease. [6] — Dec 2023 • Paper III • Q9a-b
- › Discuss nuclear medicine evaluation in epilepsy and Parkinson's disease. [5+5] — Dec 2025 • Paper III • Q5

Asked in: Dec 2020 Paper III Q2 • Jun 2021 Paper IV Q5a • Dec 2022 Paper IV Q6b • Jun 2023 Paper III Q8b • Dec 2023 Paper II Q8a-b • Dec 2023 Paper III Q9a-b • Dec 2025 Paper III Q5

Causes of movement disorders (parkinsonian syndromes and their mimics)

Table L2-01.1. Causes and their presynaptic dopaminergic status

Group	Examples	Dopamine transporter (DaT) imaging
Idiopathic Parkinson disease (PD)	Resting tremor, rigidity, bradykinesia; loss of nigrostriatal neurons	Reduced
Atypical (neurodegenerative) parkinsonism	Multiple system atrophy (MSA-P, MSA-C), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD)	Reduced
Dementia with Lewy bodies	Dementia, hallucinations, parkinsonism	Reduced
Secondary parkinsonism	Wilson disease, carbon monoxide poisoning, neuroleptic (drug-induced), vascular	Usually normal (drug-induced, vascular)
Non-degenerative mimics	Essential tremor, psychogenic parkinsonism	Normal
Huntington disease	Chorea; abnormal huntingtin protein	— (FDG: caudate/lentiform loss)

- PD affects about **1.5% of people over 65** and 2.5% over 80. Telling PD from atypical parkinsonism is clinically hard, especially when L-dopa fails.

PET and SPECT radiopharmaceuticals: mechanism, advantages, disadvantages

Table L2-01.2. Movement-disorder radiopharmaceuticals

Agent	Target / mechanism	Advantages	Disadvantages
I-123 ioflupane (FP-CIT, DaTscan), SPECT	Tropane (cocaine analogue) binding the presynaptic dopamine transporter in the striatum	Approved for essential tremor vs parkinsonian syndromes; ~90% sensitivity and specificity ; ambient light and activity do not affect it	Cannot separate PD from MSA/PSP/CBD; many drugs interfere; thyroid blockade; 3–6 h delay; US Schedule II substance
F-18 FDOPA, PET	L-dopa analogue that enters the dopamine metabolism pathway early; striatum highest, cerebellum lowest	Measures dopamine synthesis; striatal activity falls 2%–10%/year in PD	Complex: peripheral decarboxylation and methylation need carbidopa pre-treatment; tends to underestimate loss ; limited sites
C-11 / F-18 DTBZ	Vesicular monoamine transporter 2 (VMAT2)	Presynaptic integrity	Experimental
C-11 raclopride, F-18 fallypride	Postsynaptic D2/D3 receptors	Postsynaptic receptor status	Experimental
F-18 FDG, PET	Regional glucose metabolism	Pattern of cortical/subcortical change; Huntington disease	Changes in PD/atypical parkinsonism are subtle (not an approved indication in REQ)
Tc-99m HMPAO / ECD, SPECT	Regional blood flow	Available	PD shows only cortical hypoperfusion (frontal → prefrontal/parietal → all cortex)
I-123 MIBG (cardiac)	Sympathetic nerve terminals	Decreased in DLB (and PD sympathetic denervation)	Indirect, cardiac

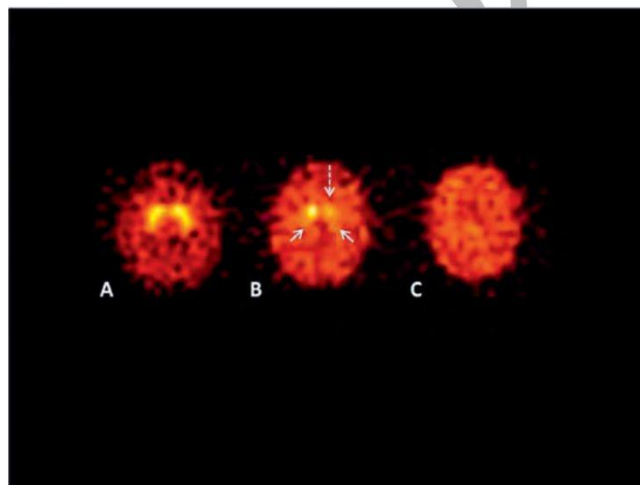
Mechanism of uptake, agent by agent

- The tracers target different steps of striatal dopamine handling: synthesis (aromatic amino-acid decarboxylase), vesicular storage (VMAT2), reuptake (presynaptic DAT) and postsynaptic receptors (D2/D1). Together they measure dopaminergic neuron integrity and loss.
- I-123 ioflupane** binds the presynaptic DAT. Its striatal density falls as nigrostriatal neurons degenerate, so the scan indirectly measures **dopaminergic terminal loss**.
 - 3–5 mCi (111–185 MBq), slow IV; SPECT at 3–6 h.
 - Thyroid blocked with potassium iodide or Lugol solution (100 mg iodide) or 400 mg perchlorate ≥1 h before; interfering drugs withheld.
- F-18 FDOPA** crosses the blood–brain barrier and accumulates most in the striatum (caudate and putamen), least in the cerebellum.
 - In plasma it is largely metabolised by **dopa decarboxylase** (to F-18 fluorodopamine) and **COMT** (to F-18 3-O-methylfluorodopa).
 - So **carbidopa** (or nitecapone) is given beforehand, and L-phenylalanine has been used to block entry of the methylated metabolite.
 - 5–10 mCi (185–370 MBq) IV; striatal uptake is **markedly reduced in PD**.
- Tc-99m HMPAO / ECD** and **F-18 FDG** are not dopaminergic. They show downstream changes in perfusion or metabolism.

I-123 ioflupane SPECT: how it is read

- Normal striata are **comma-shaped and symmetric**, with high striatal-to-background contrast.
- PD**: loss starts in the **posterior putamen**, then the anterior putamen, finally the caudate. The comma becomes a **round or oval "period"**.
 - Loss is often **asymmetric** and greater **contralateral to the worse side**.
- Atypical parkinsonism** tends to involve the **caudate earlier** and be **more symmetric**, but patterns overlap too much to separate it from PD.
- Can detect **preclinical** disease; the negative predictive value is high (97% of non-PD patients, such as essential tremor, have a normal scan).

- Changes the diagnosis in up to 30% and management in 50%–60%.
- **Visual reading** by trained readers, on a workstation that allows image manipulation, is reliable and accurate; interobserver agreement is good. Semiquantitative programs exist, but none has broad validation.



• **Fig. 3.21** Dopamine Transporter Positron Emission Tomography (PET) Imaging. PET images were obtained using ^{123}I loflupane (DaTscan). (A) Normal. Note the comma appearance of the caudate nucleus and putamen. (B) Abnormal scan in Parkinson patient with loss of putaminal activity bilaterally (*paired arrows*) and relatively decreased dopaminergic neuronal function in the left caudate nucleus (*dashed arrow*). (C) Advanced Parkinson disease with severe loss of activity in the bilateral striata.

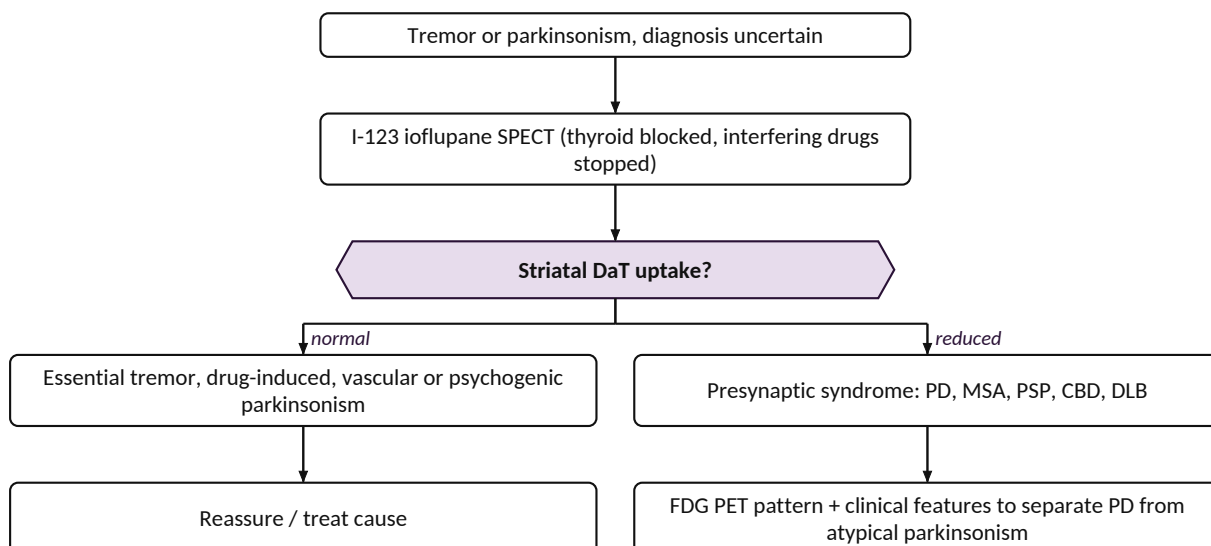
Fig. 3.21. MET 7e, p. 79.

Role in typical and atypical PD

- **Presynaptic syndromes** (PD, MSA, PSP) show reduced DaT. Vascular, drug-induced and psychogenic parkinsonism and essential tremor generally do not.
- **PD perfusion SPECT**: decreases first in the frontal cortex, then prefrontal and parietal, finally all cortex.
- **CBD on FDG**: classically affects the primary sensorimotor strip and the **ipsilateral basal ganglia or thalamus**, usually asymmetric.
- **Why it matters**: deep brain stimulation worsens **MSA**, and thalamotomy causes deterioration in **CBD**.
- **DLB**: AD-like FDG pattern plus decreased striatal DaT uptake; cardiac MIBG is also reduced.

Patient with tremor

- **Essential tremor versus PD**: DaT imaging separates them with **90% sensitivity and specificity**.
- A normal DaT scan means essential tremor, drug-induced, vascular or psychogenic tremor; an abnormal scan means a presynaptic degenerative syndrome.



Huntington disease

- FDG shows loss of metabolism in the **caudate and lentiform nuclei**, plus frontal and temporal hypometabolism. These changes **precede symptoms by many years** in gene carriers.

Current guideline (beyond the textbook)

- EANM · Procedure guidelines for brain PET imaging using [18F]FDG, version 3 (Guedj et al., Eur J Nucl Med Mol Imaging 2022;49:632–651) · 2021/2022. The textbook predates this.
- FDG PET **can differentiate PD from atypical parkinsonian syndromes**. Record whether the scan is done "off" medication (levodopa can reduce regional metabolism).
- **PD**: relative **increase** in globus pallidus/putamen, thalamus, sensorimotor cortex and cerebellum.
- **MSA**: putaminal hypometabolism (MSA-P); cerebellar hypometabolism (MSA-C).
- **PSP**: hypometabolism of caudate, thalamus, **midbrain**, frontal and medial frontal cortex.
- **CBS**: asymmetric hypometabolism of the whole striatum, frontal, sensorimotor and parietal cortex.

Pearls

- **DaT normal = no presynaptic degeneration** (essential tremor, drug-induced, vascular, psychogenic).
- PD: posterior putamen → anterior putamen → caudate; asymmetric, worse contralateral to symptoms.
- DaT cannot tell PD from MSA/PSP: use clinical features ± FDG patterns.
- Huntington: caudate hypometabolism, before symptoms.
- Dec 2025 Q5 (epilepsy part): see L3-01.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"SPECT and PET Brain Imaging", p. 63; Table 3.2, p. 74; §"Huntington Disease" and §"Parkinson Disease and Syndromes", pp. 78–79, Fig. 3.21, p. 79; Pearls & Pitfalls, p. 84.
- REQ 5e, ch. 14 "Central Nervous System", Box 14.1 and Table 14.2, e-book PDF pp. 1022, 1027; Box 14.6, pp. 1045–1046; DLB, p. 1060; CBD and Table 14.8, pp. 1071–1072; FDG in parkinsonism, p. 1075; §"Movement Disorders", pp. 1081–1082, 1084, 1087–1088 (second book: causes, F-18 FDOPA, VMAT2/D2 agents, DaT patterns, NPV and impact that MET does not give).
- SAHA 7e, ch. 13 "Diagnostic Uses of Radiopharmaceuticals in Nuclear Medicine", §"18F-Fluorodopa", p. 278 (third book: F-18 FDOPA peripheral metabolism, carbidopa pre-treatment and activity, which MET and REQ do not give).

TRODAT / DAT SPECT

› TRODAT SPECT/CT imaging — Jun 2020 • Paper III • Q5b

› 99mTc-TRODAT imaging- Patient preparation, acquisition protocol and interpretation. [7] — Dec 2021 • Paper II • Q4a

Asked in: Jun 2020 Paper III Q5b • Dec 2021 Paper II Q4a

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "TRODAT", "Tc-99m TRODAT", "Tc-99m tropine", "dopamine transporter". Checked MET ch. 3, REQ ch. 14 and SAHA ch. 7 and 13.
- Tc-99m TRODAT-1 is not described in any of the five books. The books describe the I-123 ioflupane (FP-CIT, DaTscan) dopamine-transporter SPECT, which works on the same principle.

Tc-99m TRODAT-1: the agent

- **Tc-99m TRODAT-1** is a **technetium-labelled tropine** that binds the **presynaptic dopamine transporter**, the same target as I-123 ioflupane: 2β-[N,N'-bis(2-mercaptoethyl)ethylenediaminomethyl]-3β-(4-chlorophenyl)tropine.
- **Advantage:** Tc-99m is available on site and suits the gamma camera (**140 keV**); cyclotron and I-123 tracers are costly and distance-limited.
- **Kit labelling** (single-vial formulation, about 10 µg free base): add fresh pertechnetate eluate, **heat at 100°C for 20 min**, cool 10 min at room temperature.
 - QC by HPLC and ITLC: radiochemical purity **≥85%** (typically 93%–96%), reduced hydrolysed Tc **≤5%**.
 - The labelled complex is unstable, so it is prepared on the day of the study, not in advance.

TRODAT-1: patient preparation

- No fasting; record all recent medication.
- Antiparkinsonian drugs acting on **postsynaptic receptors** do not affect TRODAT-1 uptake, so patients are studied on their **usual medication**.
- Stop **CNS stimulants** for about **4 weeks**. Drugs acting on **presynaptic transporters** are stopped for at least **7 half-lives** (e.g. tricyclics such as amitriptyline and imipramine). Long-acting SSRIs (fluoxetine) need particular care.
- Not recommended in pregnancy or during breastfeeding.

TRODAT-1: acquisition protocol

Table L2-02.1. Tc-99m TRODAT-1 SPECT protocol

Parameter	Setting
Activity	740 MBq (20 mCi) IV bolus, saline flush; some protocols 10 MBq/kg up to 900 MBq (24 mCi)
Delay	About 4 h (3.5–4 h); specific striatal binding is nearly constant from 4 h
Camera / collimator	Dual- or triple-head SPECT; LEHR parallel-hole or fan-beam collimator
Energy window	140 keV, symmetric 10% window
Acquisition	e.g. 120 projections × 60 s over 360°, 128 × 128 (about 43 min); or 60 projections per head over 180°
Processing	FBP or OSEM with a Butterworth filter; Chang attenuation correction (µ about 0.11–0.12 cm ⁻¹)

TRODAT-1: interpretation

- **Visual:** as for ioflupane. Normal striata are symmetric and comma-shaped. In PD the **putamen** is reduced first (posterior part), usually asymmetrically and contralateral to the worse side.
- **Semiquantitative:** on the 3 transverse slices with maximal striatal activity, specific binding = **(striatum – occipital) / occipital**, for striatum, caudate and putamen.
 - In healthy volunteers the striatal ratio was **1.1 ± 0.2**, with a putamen-to-caudate ratio of **0.83**. Binding falls with age (about **6%–10% per decade**) and is slightly higher in women. Each centre needs its own age-matched normal range, because values depend on the protocol.

- **Accuracy:** sensitivity similar to I-123 FP-CIT (**92% vs 95%**); specificity somewhat lower (**70% vs 86%**).
- **Dosimetry:** effective dose **0.011 mSv/MBq (men)** and **0.013 mSv/MBq (women)**, about **8–10 mSv** for 740 MBq. The **liver** is the critical organ (0.046 mGy/MBq): excretion is mainly hepatobiliary, with about 25% in urine by 28 h.

Related book material: DaT SPECT with I-123 ioflupane

Principle

- A **tropine (cocaine analogue)** with high affinity for the **presynaptic dopamine transporter (DaT)**. Striatal binding indirectly measures surviving dopaminergic nerve terminals.
- Brain uptake is 7% at 10 min and 3% at 5 h. Striatal activity is stable from 3 to 6 h. About 60% is excreted in urine by 48 h.

Patient preparation

- Review medications and **withhold drugs that interfere with binding**: cocaine, amphetamines, methylphenidate, modafinil, bupropion, sertraline, adrenergic agonists, benzotropine, fentanyl, ketamine and others.
- **Anti-parkinsonian drugs** (levodopa, dopamine agonists, MAO-B inhibitors, amantadine) do **not** interfere significantly.
- **Thyroid blockade ≥ 1 h before injection**: Lugol solution or potassium iodide (equivalent to **100 mg iodide**), or potassium perchlorate **400 mg**.
- Hydrate the patient and have them void frequently for 48 h. Ambient light and normal activity do not affect distribution.

Acquisition protocol

Table L2-02.2. I-123 ioflupane SPECT protocol

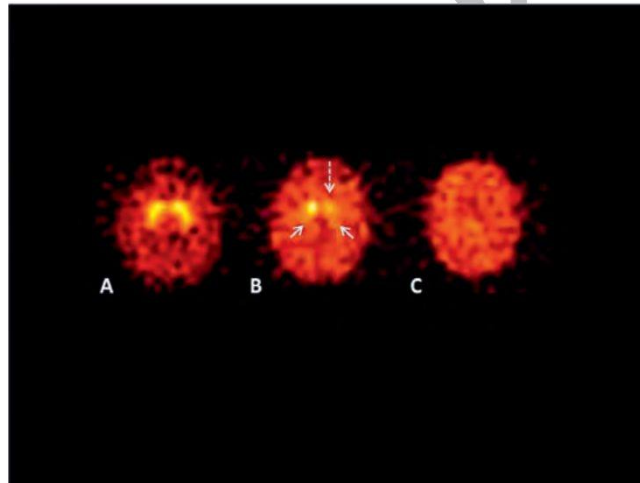
Parameter	Setting
Activity	3–5 mCi (111–185 MBq), slow IV injection, saline flush
Delay	3–6 h
Camera / collimator	Multi-head gamma camera; low-energy high-resolution
Energy window	159 keV $\pm$ 10%
Positioning	Supine, head holder beyond table end; tight orbit (11–15 cm radius)
Acquisition	3° steps, 30–40 s/step, 360° total; ≥ 1.5 million counts
Matrix	Pixel size 3.5–4.5 mm
Processing	Iterative or FBP; Butterworth low-pass filter; attenuation correction recommended (CT); reorient to AC–PC line

Interpretation

- **Visual:** intensity, shape and symmetry of the caudate and putamen.
 - Normal striata are well defined, **comma-shaped** and symmetric.
 - Abnormal striata show reduced intensity, unilateral or bilateral; the **putamen is affected more than the caudate**.
 - The comma becomes **round or oval** as its tail is lost.
- **PD:** posterior putamen → anterior putamen → caudate. Loss is often asymmetric and worse contralateral to the dominant symptoms. Ageing lowers binding only slightly.
- **Semiquantitative:** striatal binding ratio (SBR), with background in the occipital cortex.

$$\text{SBR} = (\text{mean striatal counts} - \text{mean background counts}) / \text{mean background counts}$$

- **Normal scan:** essential tremor, drug-induced, vascular or psychogenic parkinsonism. **Abnormal scan:** PD, MSA, PSP; also DLB (versus AD).
- Visual reading by trained readers on a manipulable workstation is reliable; semiquantitative methods still depend on local strategies.
- Accuracy: about 90% sensitivity and specificity for essential tremor versus PD. A negative scan effectively excludes PD (97% of non-PD patients are normal).



• **Fig. 3.21** Dopamine Transporter Positron Emission Tomography (PET) Imaging. PET images were obtained using ^{123}I ioflupane (DaTscan). (A) Normal. Note the comma appearance of the caudate nucleus and putamen. (B) Abnormal scan in Parkinson patient with loss of putamen activity bilaterally (*paired arrows*) and relatively decreased dopaminergic neuronal function in the left caudate nucleus (*dashed arrow*). (C) Advanced Parkinson disease with severe loss of activity in the bilateral striata.

Fig. 3.21. MET 7e, p. 79.

Pearls

- DaT SPECT is a **presynaptic** test: a normal scan rules out degenerative parkinsonism.
- Block the thyroid; stop stimulants, bupropion and sertraline; keep levodopa.
- "Comma → full stop": posterior putamen is lost first.
- **TRODAT-1**: 740 MBq, image at **4 h**; kit heated 100°C for 20 min; patients stay on levodopa.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"SPECT and PET Brain Imaging", p. 63; §"Parkinson Disease and Syndromes", pp. 78–79, Fig. 3.21, p. 79.
- REQ 5e, ch. 14 "Central Nervous System", I-123 ioflupane pharmacology and preparation, e-book PDF pp. 1084–1085; interpretation, pp. 1087–1088; Box 14.10 protocol and SBR, pp. 1088–1090; Box 14.11 interfering drugs, pp. 1090–1091 (second book: full protocol, drug list and SBR that MET does not give).

[4x+] L3-01 • 10 marks

Epilepsy — PET/SPECT & lesion imaging

- ▶ PET/CT imaging in epilepsy. — Jun 2020 • Paper III • Q5a
- ▶ Neuroimaging characteristics of: a) Hippocampal sclerosis b) Focal cortical dysplasia c) DNET — Dec 2020 • Paper IV • Q10a–c
- ▶ Gelastic Seizures. [2.5] — Jun 2021 • Paper III • Q6d
- ▶ Nuclear Medicine techniques and radiopharmaceuticals in the evaluation of epileptic disorders. [5] — Dec 2021 • Paper III • Q4b
- ▶ Radiopharmaceuticals being used in epilepsy. [5] — Jun 2022 • Paper II • Q7a
- ▶ Nuclear medicine imaging in epilepsy. [5] — Dec 2024 • Paper III • Q8b
- ▶ Discuss nuclear medicine evaluation in epilepsy and Parkinson's disease. [5+5] — Dec 2025 • Paper III • Q5

Asked in: Jun 2020 Paper III Q5a • Dec 2020 Paper IV Q10a–c • Jun 2021 Paper III Q6d • Dec 2021 Paper III Q4b • Jun 2022 Paper II Q7a • Dec 2024 Paper III Q8b • Dec 2025 Paper III Q5

Why nuclear medicine in epilepsy

- About **25%** of patients with epilepsy do not respond to drugs and develop **intractable seizures**. In refractory partial (focal) epilepsy, **surgical removal of the seizure focus** can help.
- PET and SPECT localise the epileptogenic focus non-invasively when **MRI shows no lesion**, or when the lesion does not match EEG and clinical findings.
 - This matters especially under **2 years of age**, where immature myelination limits MRI.
- EEG localises the ictal focus in only about 50% of patients and mislocalises it in 5%–10%. The nuclear studies guide **intracranial EEG grid placement** and surgery.
- If the focus is confined to a temporal lobe, about **70%** of patients improve or become seizure-free after partial temporal lobectomy.

Principle

- **Ictal** (during a seizure): the focus shows **increased perfusion and metabolism**.
- **Interictal** (between seizures): **decreased (or normal)** perfusion and metabolism.
- **Postictal**: mixed increases and decreases. So the clinical and EEG state at the moment of injection must be known; continuous EEG monitoring is best.

Radiopharmaceuticals and techniques

Table L3-01.1. Nuclear medicine techniques in epilepsy

Technique	Radiopharmaceutical	Finding at the focus	Sensitivity (temporal lobe)
Ictal SPECT (method of choice for perfusion)	Tc-99m HMPAO or Tc-99m ECD	Hyperperfusion (may include surrounding hypoperfusion)	85%–95% (about 90%); extratemporal 50%–75%
Interictal SPECT	Tc-99m HMPAO or ECD	Hypoperfusion (often lateral > mesial temporal)	<50% (MET); about 70% (REQ)
Interictal FDG PET (method of choice for metabolism)	F-18 FDG	Hypometabolism , larger than the focus	70%–80% (MET); about 80%, higher with an MRI lesion (REQ)
Ictal FDG PET	F-18 FDG	Increased, diffuse	Rarely feasible; unreliable
Receptor PET/SPECT	C-11 flumazenil, I-123 iomazenil (benzodiazepine receptor); C-11 carfentanil (mu opiate receptor)	Used to detect seizure foci / quantify receptors in temporal lobe epilepsy	Research use

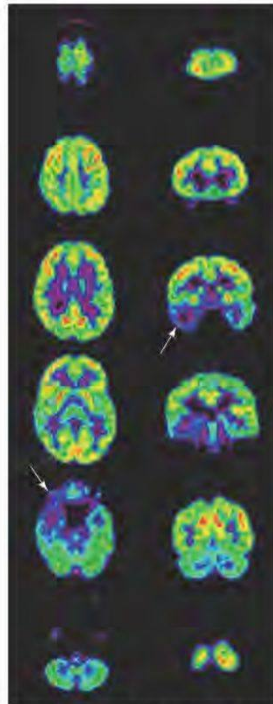
Ictal SPECT

- Patient admitted and continuously monitored with EEG, off medication. The tracer is kept **at the bedside** and injected **during the seizure or within 30 s of its end** (within seconds of onset).
- HMPAO and ECD are **trapped** in the brain on first pass. Imaging can therefore wait a few hours until the seizure is controlled.

- Activity: Tc-99m ECD 25–30 mCi (875–1110 MBq) for the baseline (interictal) scan; SPECT 10–15 min after injection, likewise after the ictal injection.

Interictal FDG PET

- Fast 4–6 h, glucose <200 mg/dL; F-18 FDG 8 mCi (296 MBq), quiet dim room; uptake 35–60 min.
- If sedation is needed, give it >20 min after injection.
- **EEG during injection and uptake** detects subclinical seizures. An unrecognised seizure raises uptake on the lesion side, making the **normal contralateral lobe look falsely hypometabolic**.
- Hypometabolism is usually **larger than the epileptogenic focus**. It is used for **lateralisation and general location**, not exact surgical margins.
- FDG PET is superior to interictal SPECT.

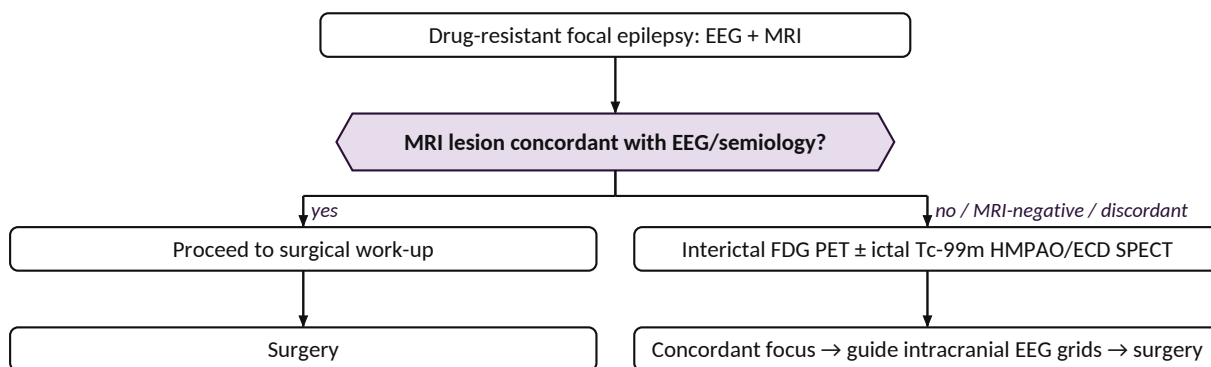


• **Fig. 3.15** Epilepsy (Interictal Study). Axial and coronal ^{99m}Tc-HMPAO brain perfusion images obtained between seizures show characteristically decreased activity in the right temporal lobe (arrows).

Fig. 3.15. MET 7e, p. 72.

PET/CT and SPECT findings by epilepsy type

- **Mesial temporal lobe epilepsy** (the most common complex partial epilepsy):
 - interictal temporal hypometabolism or hypoperfusion;
 - may be bilateral but asymmetric, or with **ipsilateral frontal** reduction.
- **Extratemporal epilepsy**:
 - interictal hypometabolism or hypoperfusion is **uncommon** when CT/MRI is negative;
 - ictal SPECT is harder because seizures are brief and spread fast;
 - a malformed cortex may show extensive or multifocal change without a resectable focus.
- **Paediatric conditions**:
 - **Epileptic spasms**: focal FDG hypometabolism without an MRI correlate may be resectable.
 - **Tuberous sclerosis**: 80%–90% have seizures. Interictal FDG is low in **all** tubers; **ictal SPECT** (with SPECT/CT) identifies the offending tuber.
 - **Neonatal seizures**: FDG PET can show a focal abnormality while CT/MRI are negative or equivocal.
- **Diaschisis**: remote change can accompany a focus, e.g. increased cerebellar uptake on ictal images in a patient with a malformed cortex. Recognise it; do not call it a second lesion.



Neuroimaging characteristics asked: hippocampal sclerosis, focal cortical dysplasia, DNET, gelastic seizures

- **Hippocampal (mesial temporal) sclerosis** is the **most common pathology of seizure foci** (gliotic temporal scarring). MRI often shows **mesial temporal hippocampal sclerosis**. On nuclear imaging: interictal temporal hypometabolism or hypoperfusion and ictal temporal hyperperfusion.

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "cortical dysplasia", "focal cortical dysplasia", "DNET", "dysembryoplastic", "gelastic", "hypothalamic hamartoma". Checked MET ch. 3, REQ ch. 14 and SAHA ch. 13.
- The imaging features of focal cortical dysplasia and DNET, and gelastic seizures, are not described in any of the five books. Related material: a **congenitally malformed cortex** can show extensive interictal hypoperfusion and widespread ictal hyperperfusion without a resectable focus (REQ).

Current guideline (beyond the textbook)

- EANM · Procedure guidelines for brain PET imaging using [18F]FDG, version 3 (Guedj et al., Eur J Nucl Med Mol Imaging 2022;49:632–651) · 2021/2022. The textbook predates this.
- Indication: presurgical evaluation of **focal pharmaco-resistant epilepsy** in adults and children, with **interictal** injection.
- FDG PET is **more sensitive than interictal perfusion SPECT**, especially in temporal lobe epilepsy. In extratemporal epilepsy it identifies the epileptogenic zone in **38%–67%**.
- Interictal hypometabolism corresponds to the **entire irritative zone**. Limited hypometabolism predicts a better surgical outcome.

Pearls

- **Ictal = hot** (perfusion SPECT, inject within 30 s); **interictal = cold** (FDG PET).
- Ictal SPECT is the most sensitive test (85%–95% temporal); interictal SPECT is the least (<50%).
- Run EEG during FDG uptake: a hidden seizure makes the normal side look cold.
- Tuberous sclerosis: FDG marks every tuber; **ictal SPECT finds the epileptogenic one**.
- Dec 2025 Q5 (Parkinson part): see L2-01.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Epilepsy" (ictal and interictal imaging, extratemporal, paediatric), pp. 71–72, Fig. 3.15, p. 72; Pearls & Pitfalls, pp. 83–84.
- REQ 5e, ch. 14 "Central Nervous System", Box 14.2 FDG protocol, e-book PDF pp. 1034–1035; §"Seizures", pp. 1090, 1092; Fig. 14.30, p. 1098 (second book: EEG limitations, injection logistics, updated sensitivities and malformed cortex).
- SAHA 7e, ch. 13 "Diagnostic Uses of Radiopharmaceuticals in Nuclear Medicine", Tc-99m ECD ictal/interictal protocol, p. 273; F-18 FDG in epilepsy, p. 277; receptor ligands (C-11 carfentanil, C-11 flumazenil, I-123 iomazenil), pp. 281–282 (third book: ECD activity and receptor tracers, which MET and REQ do not give).

L4 Other neurological applications

[1×] L4-01 • 5 marks

Role of PET in imaging of auto-immune encephalitis. [5]

Asked in: Jun 2023 Paper IV Q6a

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "autoimmune encephalitis", "autoimmune", "limbic", "encephalitis", "paraneoplastic", "NMDA". Checked MET ch. 3, REQ ch. 14 and SAHA ch. 13.
- Autoimmune encephalitis is not described in any of the five books.
- 'Autoimmune' occurs only for thyroid, transplant and general inflammatory conditions (MET ch. 4, 10, 12; REQ ch. 8, 10, 11).

Related book material: FDG brain PET

- FDG uptake reflects **regional glucose metabolism**, not blood flow. FDG PET is a physiological test that can show disease **before morphological change on CT or MRI**.
- Normal brain: basal ganglia (putamen, caudate) and thalami highest, then cortical grey matter; white matter very low.
- **Drugs alter global and regional metabolism**: sedatives, antiepileptics, neuroleptics and barbiturates.
 - **Corticosteroids decrease brain glucose metabolism**, which matters when patients are already on steroids.
- Disease states can **increase or decrease** brain FDG uptake. Interpretation must therefore look for regional hypermetabolism as well as hypometabolism.
- Inject in a quiet, dim room, patient awake with eyes open.

Current guideline (beyond the textbook)

- EANM • Procedure guidelines for brain PET imaging using [18F]FDG, version 3 (Guedj et al., Eur J Nucl Med Mol Imaging 2022;49:632–651) • 2021/2022. The textbook predates this.
- **Indication**: encephalitis, including autoimmune encephalitis (AE). FDG PET is **especially relevant when MRI is negative or inconclusive**.
- **Typical pattern**: global hypometabolism with relative striatal and limbic hypermetabolism.
 - Sensitivity 80%–90% (meta-analysis); specificity 82% against MCI.
 - **Medial temporal changes** are linked preferentially to antibodies against **intracellular antigens**.
- **Normalisation** of intensity is critical, because hyper- and hypometabolic regions coexist.
- **Scan before starting corticosteroids** where clinically possible (risk of false negatives).
- **Whole-body FDG PET** looks for an underlying cancer in paraneoplastic syndromes. The metabolic profile is used to **monitor treatment response**.

Pearls

- FDG brain PET is a physiological test: it can be abnormal **before CT/MRI change**.
- **Corticosteroids lower brain glucose metabolism**: record steroid use.
- Read for regional **hypermetabolism as well as hypometabolism**.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"SPECT and PET Brain Imaging" and §"PET/CT Image Interpretation", p. 63; §"Brain Tumors" (corticosteroids decrease brain glucose metabolism), p. 68.

Diamox SPECT. [5]

Asked in: Jun 2023 Paper III Q5b

Principle

- **Acetazolamide (Diamox)** is a **carbonic anhydrase inhibitor**. It raises tissue CO_2 and causes cerebral **vasodilatation**; normal cerebral blood flow increases **three- to fourfold**.
- Distal to a significant stenosis, autoregulatory vasodilatation is **already maximal**. These territories cannot respond, so blood is shunted away.
- After Diamox they appear as **relative perfusion defects** on SPECT, compared with surrounding normal brain and with the baseline study. In effect it is a **cerebrovascular "stress test"**, analogous to dipyridamole myocardial perfusion imaging.
- Most patients with TIAs or carotid stenosis show **no cortical defect at rest**. The challenge unmasks **diminished cerebrovascular reserve**.

Indications

- Evaluation of cerebrovascular reserve:
 - transient ischaemic attack and completed stroke;
 - atherosclerotic (carotid) stenosis;
 - vascular malformations and anomalies;
 - **moyamoya**;
 - stroke-risk evaluation in these groups.

Contraindications and cautions

- **Sulfa allergy**.
- Usually avoided within the **first 3 days after an acute stroke**.
- Acetazolamide is also listed as a cause of **false-positive cisternogram** results.

Protocol

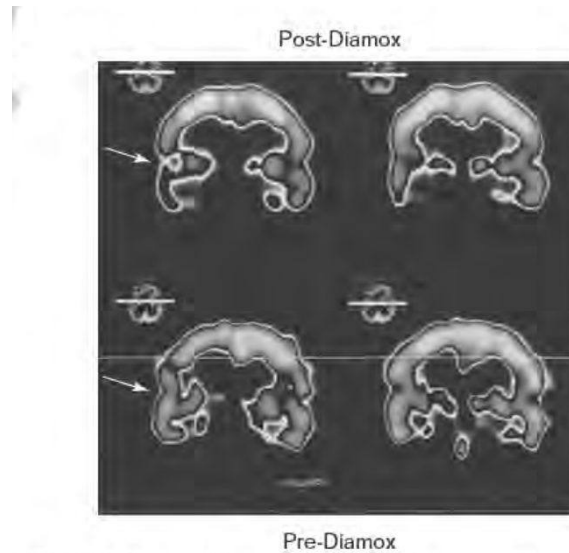
Table L4-02.1. Diamox SPECT protocol

Step	Detail
Radiopharmaceutical	Tc-99m HMPAO or Tc-99m ECD; inject in a quiet, dimly lit room, eyes and ears open, IV access placed ≥ 10 min before
Acetazolamide dose	1000 mg in 10 mL sterile water, slow IV push over 2 min; children 14 mg/kg
Timing	Wait 10–20 min after acetazolamide, then inject the tracer
Order	Challenge study first; if normal, the baseline (rest) study may be omitted. If abnormal, compare with a rest study
Same-day option	Pre-ACZ Tc-99m ECD 15 mCi (555 MBq); ACZ 1 g given during the first scan; then Tc-99m ECD 25 mCi (850 MBq) and post-ACZ SPECT 15 min later
Imaging	Multi-head SPECT, high-resolution collimator; ask the patient to void before acquisition

- The acetazolamide effect begins within 10 min, peaks at 25 min and fades within 1 h.

Interpretation

- **Normal**: global increase in perfusion, with no new regional defect.
- **Reduced reserve**: a region that is normal or mildly reduced at rest becomes a **relative defect after Diamox**. These territories are at **highest risk of infarction**.
- **Semiquantitative**: ROIs around the cortex (clock-face) give rest and post-Diamox count profiles. A dip on the post-Diamox curve marks the non-responding territory.
- **Always compare** the stress study with the rest study.



• **Fig. 3.8** Diamox Challenge Study. Post- and pre-Diamox coronal SPECT brain perfusion images show decreased vascular reserve (decreased perfusion) in the right temporal region (arrows) after Diamox administration. (Case courtesy B. Barron, MD and Lamk Lamki, MD.)

Fig. 3.8. MET 7e, p. 67.

Pearls

- Diamox = cerebral "dipyridamole": normal CBF $\uparrow$ 3–4 $\times$; stenosed territories cannot dilate.
- 1 g IV over 2 min (14 mg/kg in children); tracer 10–20 min later.
- Avoid with sulfa allergy and in the first 3 days after acute stroke.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Carotid Stenosis", p. 67, Fig. 3.8, p. 67; Pearls & Pitfalls, p. 84; Appendix E (brain perfusion SPECT; acetazolamide challenge; cisternogram), p. 489; Appendix F, p. 512.
- REQ 5e, ch. 14 "Central Nervous System", §"Cerebrovascular Disease" (acetazolamide SPECT), e-book PDF pp. 1100–1102 (second book: moyamoya and other indications, CO₂ mechanism and semiquantitative analysis).
- SAHA 7e, ch. 13, §"Brain Interventional Study", p. 282 (third book: time course of the acetazolamide effect and same-day split-dose protocol).

[1 $\times$] L4-03 • 5 marks

Role of Nuclear Medicine in the evaluation of drug addiction. [5]

Asked in: Jun 2021 Paper III Q2a

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "addiction", "drug abuse", "substance abuse", "cocaine", "opiate/opioid", "alcohol". Checked MET ch. 3, REQ ch. 14 and SAHA ch. 13.
- None of the books discusses the role of nuclear medicine in the evaluation of drug addiction.
- 'Drug abuse', 'cocaine' and 'alcohol' occur only as risk factors for infection, as interfering drugs for DaT and MIBG imaging and as causes of dementia (MET ch. 3, 7–8; REQ ch. 13–14).

What nuclear imaging measures in addiction

- PET and SPECT show **how fast a drug reaches the brain, which target it occupies**, and the **long-term changes** addiction produces.
- **Tracers:**
 - **C-11 raclopride:** vacant D₂/D₃ receptors (lower binding = fewer receptors or more dopamine release).
 - **F-18 FDG:** regional glucose metabolism.
 - **C-11 d-threo-methylphenidate (PET)** and **I-123 β -CIT (SPECT):** the dopamine transporter.
 - **C-11 carfentanil:** mu opioid receptors.
 - **F-18 2-FA:** α 4 β 2 nicotinic receptors.

Key findings

- **Speed of entry determines reward:** fast IV stimulants raise striatal dopamine with a "high"; slow oral methylphenidate is not reinforcing.
- **Low striatal D2 receptors** in **cocaine, alcohol, methamphetamine, heroin and nicotine** users. The loss persists months after detoxification for cocaine, alcohol and methamphetamine; detoxified cannabis users show no significant difference.
- **Blunted dopamine release:** IV methylphenidate-induced dopamine release is **at least 50% lower** in cocaine abusers and alcoholics than in controls.
- **Frontal hypometabolism (FDG)** in the **orbitofrontal, cingulate and dorsolateral prefrontal cortex**, tracking low D2: a likely basis of impaired inhibitory control.
- **Cue reactivity:** drug cues raise dorsal striatal dopamine in cocaine abusers, in proportion to craving.
- **Neurotoxicity and recovery:** methamphetamine abusers lose DAT, with partial recovery after **12–17 months** of abstinence (caudate +19%, putamen +16%).
- **Opioid receptors: increased mu opioid receptor binding** in cocaine users, correlating with craving and relapse.
- **Nicotine:** 1–2 puffs occupy **50%** of $\alpha 4\beta 2$ receptors for about 3 h, and a full cigarette **>88%**. Smokers' brains show **40%** less MAO-B.

Vulnerability

- High D2 receptor levels may **protect:** unaffected members of alcoholic families have higher striatal D2.

Related book material

Perfusion imaging

- **Cocaine abuse** can produce **multiple small cerebral perfusion defects** on SPECT, as can multi-infarct dementia and vasculitis.

Dopamine transporter imaging and drugs of abuse

- I-123 ioflupane and the other tropane DaT agents (C-11/F-18 β -CIT) are **derived from cocaine**. They bind the same presynaptic dopamine transporter.
 - I-123 ioflupane is a **Schedule II controlled substance** in the United States.
- Drugs of abuse **interfere with DaT binding** and must be stopped before a DaT scan: **cocaine, amphetamines (d-amphetamine, methamphetamine), methylphenidate**, other CNS stimulants, opioids (fentanyl), ketamine and PCP.

Receptor PET agents (experimental)

Table L4-03.1. Neuroreceptor PET agents listed in the books

Agent	Target
C-11 carfentanil	Mu opiate receptor
F-18 FDPN	Opiate receptor (nonspecific)
C-11 raclopride, F-18 fallypride	Postsynaptic D2/D3 dopamine receptor
C-11 / F-18 DTBZ	Vesicular monoamine transporter 2
C-11 flunitrazepam	Benzodiazepine receptor
C-11 N-methylspiperone	D2 receptor density

- These agents quantify the neurotransmitter systems that drugs of abuse act on. In the books they are listed as experimental (research) tools.

Pearls

- Cocaine use: multiple small perfusion defects on brain SPECT.
- Stimulants, cocaine and opioids interfere with DaT (ioflupane) binding: ask about drug use before DaT imaging.
- C-11 carfentanil = mu opiate receptor; C-11 raclopride = D2/D3 receptor.
- Addiction = **low D2 + blunted dopamine release + orbitofrontal hypometabolism**.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Parkinson Disease and Syndromes" (ioflupane, cocaine analogue, Schedule II), p. 78; Pearls & Pitfalls, p. 83.
- REQ 5e, ch. 14 "Central Nervous System", Table 14.2, e-book PDF p. 1027; tropane DaT agents, p. 1084; Box 14.11 interfering drugs, p. 1091 (second book: receptor agents and drug interactions).
- SAHA 7e, ch. 13, §"Other Radiopharmaceuticals", pp. 281–282 (third book: C-11 N-methylspiperone and C-11 carfentanil).

[1×] L4-04 • 5 marks

Radionuclide Cysternography. [5]

Asked in: Jun 2022 Paper II Q4a

Principle

- About 400–500 mL/day of CSF is formed, mainly by the choroid plexus. The total volume is 120–150 mL (about 40 mL in the ventricles).
- CSF leaves the fourth ventricle, flows up through the subarachnoid spaces to the cerebral convexities, and is resorbed in the **arachnoid villi**.
- A tracer **miscible with CSF**, which stays in the CSF compartment until absorbed, is given **intrathecally**. It must be non-toxic, **sterile and pyrogen-free**.

Indications

- **Communicating (normal-pressure) hydrocephalus**.
- **CSF leak** (rhinorrhoea or otorrhoea), especially when CT/MR cisternography is inconclusive or the leak is intermittent.
- **CSF shunt patency**.

Radiopharmaceutical and technique

- **In-111 DTPA** ($T_{1/2}$ 2.8 days; photopeaks 171 and 245 keV): **0.5 mCi (18.5 MBq)**.
 - Lumbar puncture with a small-bore (22-gauge) needle into the subarachnoid space.
 - Postpone about **1 week after a recent lumbar puncture** to limit leakage.
- **Tc-99m DTPA** (1–3 mCi, 37–111 MBq) is preferred for **shunt studies**, which are short.
- **Imaging**: medium-energy collimator.
 - Spine at 2–4 h to confirm a successful injection.
 - Head: anterior, posterior and lateral views at **6, 24 and 48 h**, and 72 h if needed.
 - SPECT/CT if the planar images are equivocal.

Normal cisternogram

- Activity reaches the **basal cisterns at 2–4 h**, then the sylvian and interhemispheric cisterns (an anterior "**trident**").
- By **24 h**: complete ascent over the **convexities and parasagittal region**.
- **No ventricular entry**. Transient entry at 4 h that clears by 24 h is of doubtful significance.

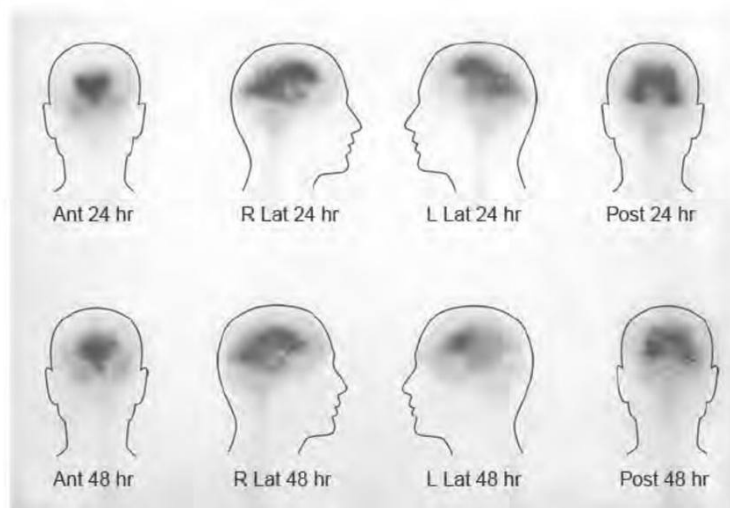
Normal-pressure hydrocephalus

- **Clinical triad**: ataxia, dementia and urinary incontinence. Hydrocephalus without significant atrophy on CT, with normal CSF pressure.
- **Classic pattern**:
 - **early ventricular entry at 4–6 h**;
 - **persistence of ventricular activity at 24, 48 and even 72 h** (a central heart-shaped image);
 - **delayed or absent ascent** over the convexities.
- Mixed patterns are of doubtful value in diagnosing NPH or predicting response to shunting.

Table L4-04.1. Cisternographic flow patterns (REQ Table 14.9)

Type	Pattern	Cause
I	Tracer over convexities by 24 h	Normal; non-communicating hydrocephalus
II	Delayed convexity ascent, no ventricular reflux	Cerebral atrophy, old age
IIIA	Transient ventricular reflux, convexities reached by 24 h	Indeterminate: evolving or resolving communicating hydrocephalus
IIIB	No convexity activity, transient ventricular reflux	NPH
IV	No convexity activity, persistent ventricular reflux	NPH

- **Limitations:** the patterns are **not specific** for predicting response to shunting. Lumbar puncture can cause headache (>25%–30%), infection or CSF leak.



• **Fig. 3.23** Normal-Pressure Hydrocephalus. Anterior (*Ant*), lateral (*Lat*), and posterior (*Post*) images of the head performed at 24 and 48 hours. The images do not show the usual trident pattern but rather a central, heart-shaped structure representing activity in the lateral ventricles. The activity more laterally and lower represents activity in the sylvian fissures. Even at 48 hours, activity has not ascended over the superior aspect of the convexities as would normally be expected by 24 hours, and there is persistence of activity within the lateral ventricles centrally.

Fig. 3.23. MET 7e, p. 81.

CSF leak

- Sensitivity **50%–100%**, specificity close to **100%**.
- Common sites:
 - cribriform plate and ethmoid sinuses;
 - sella into sphenoid sinus;
 - sphenoid ridge into the ear.
- Image **at 1–3 h**, when activity reaches the basal cisterns, in the projection and position that provoke the leak.
- **Pledgets** placed before injection are removed **4–24 h** later and counted in a well counter with a serum sample (counts per gram). A **pledget-to-serum ratio >1.5** indicates a leak.
- Counting the pledgets is more sensitive than imaging.

Shunt patency

- Tracer injected into the **shunt reservoir** under aseptic conditions.
- A **patent distal limb** clears the reservoir with a half-time **usually <10 min**, and activity spreads freely through the peritoneum (or reaches the right atrium).
- **Manual occlusion of the distal limb** during injection refluxes tracer into the ventricles. This tests the proximal limb.
- Focal pooling at the catheter tip suggests **entrapment by adhesions**.

Pearls

- In-111 DTPA intrathecal 0.5 mCi (18.5 MBq): images at 6, 24, 48 (72) h.
- NPH = **early ventricular entry** + **persistence** + **no convexity ascent** (type IV).
- CSF leak: pledget-to-serum ratio >1.5; image at 1–3 h.

Sources

- MET 7e, ch. 3 "Central Nervous System", §"Cerebrospinal Fluid Imaging" (radiopharmaceuticals, normal examination, NPH, leaks, shunt patency), pp. 79–83, Fig. 3.23, p. 81; Pearls & Pitfalls, p. 84; Appendix E (cisternogram), pp. 489–490.
- REQ 5e, ch. 14 "Central Nervous System", §"Cerebrospinal Fluid Imaging", e-book PDF pp. 1111, 1115–1120, 1123; Table 14.9, p. 1119 (second book: In-111 photopeaks, flow-pattern classification and limitations).

PART 7

Thyroid & Parathyroid Imaging

F1 Thyroid physiology & function tests

[1×] F1-01 • 10 marks

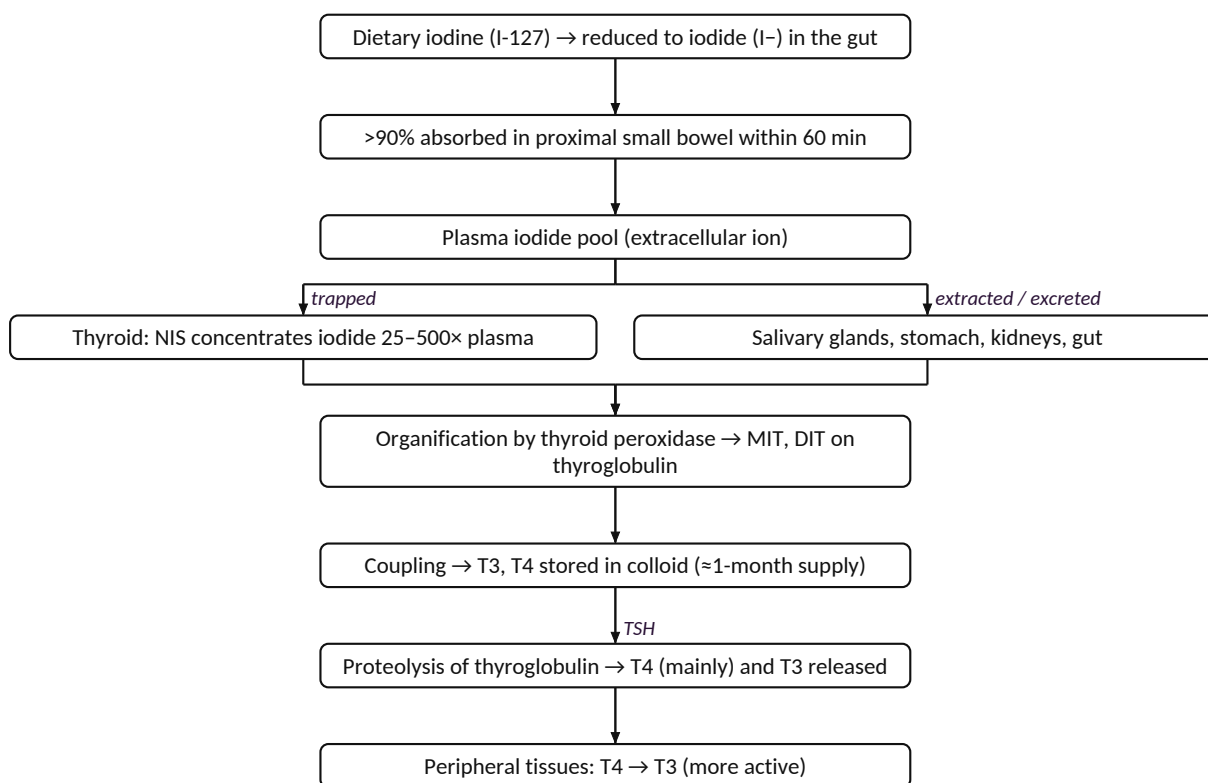
Discuss the iodine cycle in human body. [10]

Asked in: Dec 2024 Paper I Q8

Overview

- Thyroid imaging and uptake tests exploit successive steps of **thyroid hormone synthesis**. Radioiodine follows stable dietary iodine exactly through the cycle.
- The cycle: **intake** → **absorption** → **plasma iodide pool** → **thyroid trapping** → **organification** → **coupling** → **storage in colloid** → **TSH-driven release** → **peripheral conversion** → **excretion**, with **TSH feedback** regulating the thyroid steps.

Flowchart F1-01.1. The iodine cycle (MET ch. 4; REQ ch. 8)



1. Intake and absorption

- Ingested iodine is **reduced to iodide (I-)** in the proximal small intestine. **More than 90% is absorbed within 60 minutes.**
- It is detectable in the thyroid within minutes and reaches the **follicular lumen** by **20–30 minutes**.

2. Distribution: the plasma iodide pool

- Iodide circulates as an **extracellular ion**. It leaves the blood by **thyroid and gastric extraction**, then **urinary and intestinal excretion**.
- Salivary glands, stomach and choroid plexus** take up radioiodine but do **not concentrate or retain** it.
- Size of the pool** governs fractional uptake:

- **High dietary iodide** (or iodinated contrast) dilutes radioiodine, so uptake falls.
- An "**iodide-starved**" **gland** traps more, so uptake rises.
- **Chronic renal failure** retains iodide, enlarges the stable pool and lowers uptake.

3. Trapping (iodide transport)

- Iodide is **actively transported** into the follicular cell by the glycoprotein **sodium iodide symporter (NIS)**: the first step of hormone synthesis.
- The "thyroid pump" concentrates iodide **25–500 times** the plasma level.
- Trapping is **blocked competitively by monovalent anions** (e.g. potassium perchlorate).
- **Tc-99m pertechnetate** is **trapped but not organified**: it slowly washes out unaltered. Only **1%–5%** of the injected activity is trapped.

4. Organification and coupling

- At the follicular cell–colloid interface, **thyroid peroxidase** oxidises iodide to iodinium/neutral iodine. This binds **tyrosyl residues of thyroglobulin** to form **monoiodotyrosine (MIT)** and **diiodotyrosine (DIT)**.
- **Coupling** of iodotyrosines forms **T3 and T4**, still bound to thyroglobulin.
- Organification is **inhibited by PTU and methimazole**. It is defective in **congenital organification defects** and **Hashimoto thyroiditis**.

5. Storage

- Hormone-laden thyroglobulin is **stored in the colloid** of the follicular lumen.
- The normal gland holds about a **1-month supply**, so drugs that block synthesis take effect only after stores are depleted.

6. Release and peripheral metabolism

- **TSH** stimulates iodide uptake, organification and **thyroglobulin hydrolysis by proteolytic enzymes**, releasing hormone into the blood.
- **T4** is the main hormone released. It is carried by **thyroid-binding proteins** and **converted peripherally to the more active T3**.
- **Thyroglobulin itself is not released**, except in disease (thyroiditis, thyroid cancer).

7. Regulation: thyroid–pituitary feedback

- Low circulating T4/T3 increases hypothalamic **TRH** and pituitary **TSH**; high levels suppress them.
- In hyperthyroidism TSH is suppressed; in hypothyroidism it rises.

8. Excretion

- Iodide is excreted by the **kidneys** and the **gastrointestinal tract**.

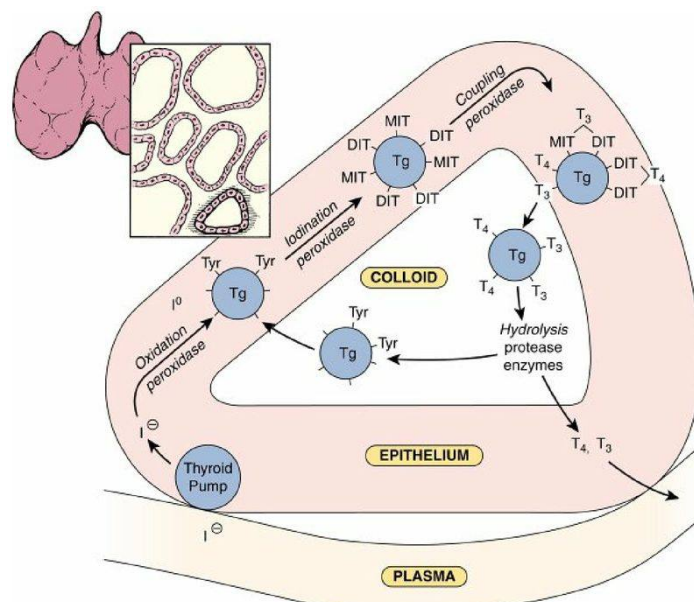


FIG. 8.2 Iodine metabolism. The thyroid follicular cell epithelium extracts (traps) iodide from the plasma via the sodium iodide symporter (thyroid pump) and organifies it. Iodide (I^-) is converted to neutral iodine (I_0), which is then incorporated into thyroglobulin-bound tyrosine molecules as monoiodotyrosine (MIT) or diiodotyrosine (DIT). Coupling of the iodotyrosines results in T_4 and T_3 hormone bound to the thyroglobulin, which is transported to and stored in the colloid, until T_4 and T_3 are released into the plasma by proteolytic enzymes. T_4 is converted to the more active T_3 peripherally.

Fig. 8.2. REQ 5e, e-book PDF p. 464.

Table F1-01.1. Steps of the iodine cycle and how nuclear medicine probes or blocks them

Step	Site / mechanism	Clinical and nuclear-medicine relevance
Absorption	Proximal small bowel, >90% in 60 min	Fast 2–4 h before an oral dose; vomiting or diarrhoea impair absorption
Plasma pool	Extracellular iodide	Diet, contrast and renal failure change fractional uptake
Trapping	NIS	Imaged by Tc-99m pertechnetate; blocked by perchlorate; basis of radioiodine uptake in DTC
Organification	Thyroid peroxidase	Requires radioiodine (not Tc-99m) to image; blocked by PTU/methimazole
Storage	Colloid	~1-month supply: antithyroid drugs act slowly
Release	TSH-driven proteolysis	Radioiodine uptake rises with TSH; TSH >30 needed before DTC scans
Feedback	TRH–TSH axis	Low uptake in thyroiditis reflects intact feedback, not a damaged pump

Conditions that shift the cycle (MET Box 4.1)

- **Increased uptake:** hyperthyroidism (diffuse or nodular goiter), early Hashimoto thyroiditis, recovery phase of subacute thyroiditis, **rebound** after abrupt withdrawal of antithyroid drugs or thyroid hormone, enzyme defects, **iodine deficiency**, hypoalbuminaemia, exogenous TSH, tumour-secreted stimulators (gonadal and chorionic origin), pregnancy.
- **Decreased uptake:** hypothyroidism, **iodine overload** (especially radiographic contrast), interfering medications, subacute or autoimmune thyroiditis, thyroid hormone therapy, ectopic hormone secretion from tumours (struma ovarii, functioning metastases), renal failure.
- **β-blockers** (e.g. propranolol) do not affect gland function and do not alter radioiodine uptake.
- The **absorbed thyroid dose** from radioiodine depends on gland size, the **biological half-life of iodine in the gland**, the **size of the iodine pool** and the spatial distribution of iodine. Together these can change the dose up to 10-fold.

Measuring the cycle: radioiodine uptake

- **Normal 24-h uptake about 10%–30%**, and **4–6-h uptake about 5%–15%**, in both children and adults.

- With **rapid turnover** (Graves disease) or **defective organification** (congenital defect, antithyroid drugs, Hashimoto), the 4–6-h uptake can exceed the 24-h value.
- **Placental and breast-milk transfer:** radioiodine crosses the placenta, the **fetal thyroid accumulates iodine from about the 12th week of gestation**, and it is secreted in breast milk.

Pearls

- **Trapping (NIS) vs organification (TPO):** Tc-99m shows trapping only; radioiodine shows both.
- NIS concentrates iodide **25–500×**; **perchlorate** blocks trapping; **PTU/methimazole** block organification.
- **>90% absorbed in 60 min;** follicular lumen reached in 20–30 min; normal 24-h RAIU **10%–30%**.
- Iodine load and renal failure enlarge the stable pool, so uptake falls.
- T4 is the main secreted hormone; **T3 is formed peripherally**.

Sources

- MET 7e, ch. 4 "Thyroid, Parathyroid, and Salivary Glands", §"Thyroid Radioiodine Uptake and Imaging" and §"Radiopharmaceuticals", pp. 85–86; §"Radioiodine Uptake Test", §"Factors Affecting Iodine Uptake", pp. 86–88; Box 4.1, p. 88; §"Thyroid Gland Imaging", p. 89.
- REQ 5e, ch. 8 "Endocrine System", §"Thyroid Anatomy and Physiology" and §"Radiopharmaceuticals", e-book PDF pp. 461–464 (Fig. 8.2) and p. 467 (Fig. 8.3 caption, TRH–TSH feedback); §"Subacute Thyroiditis", pp. 487–488; Box 8.2, p. 471 (second book: absorption, NIS concentration ratio, storage, release, peripheral conversion and feedback, which MET does not describe).

[1×] F1-02 • 5 marks

What is Perchlorate discharge test? Why its use has been drastically reduced in current time?
[3+2]

Asked in: Dec 2021 Paper II Q2b

NOT COVERED IN SOURCE

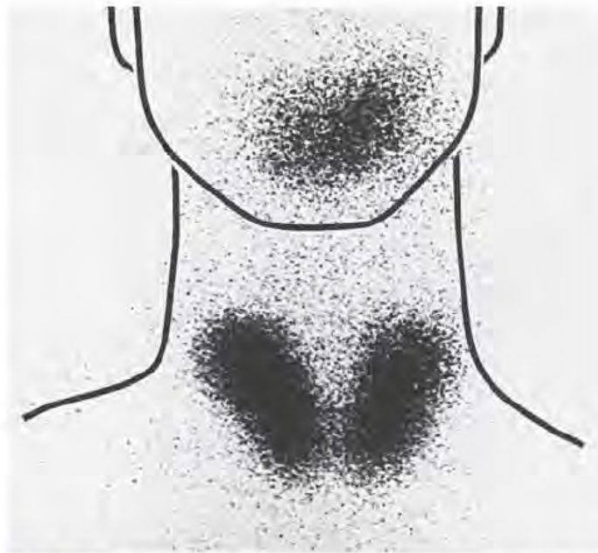
- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "perchlorate discharge", "discharge test", "perchlorate washout", "washout test", "perchlorate", "organification defect", "Pendred", "dyshormonogenesis". Checked MET ch. 4 and REQ ch. 8.
- The perchlorate discharge test, its protocol and the reasons for its decline are not described in any of the five books. Related material follows.
- Perchlorate occurs only as a thyroid- or gastric-blocking agent and as an interfering drug (MET pp. 78, 88, 114; REQ ch. 8, 10, 14; SAHA ch. 13), never as a discharge test.

Related material in the books: the physiology the test relies on

- **Trapping vs organification:** iodide is actively trapped by the **sodium iodide symporter**, then oxidised by thyroid peroxidase and bound to thyroglobulin (**organification**).
- **Perchlorate** is a **monovalent anion** that blocks trapping and uptake **competitively**. Oral perchlorate or SSKI blocks radioiodine accumulation with efficacy **approaching 100%** if given before the radioiodine, and retains some effect up to 12 h later.
- **Without organification**, trapped iodide is not bound and **washes out of the gland**.

Related material: organification defects and how the books detect them

- **Congenital organification defects** (autosomal recessive defects of iodide oxidation and organification) cause about **15% of congenital hypothyroidism**. The infant has low thyroid hormone and high TSH.
- **24-h radioiodine scan:** usually **no thyroid activity**, because the trapped iodine washes out. This cannot be told apart from an absent gland.
- **Tc-99m pertechnetate scan or 2–4-h I-123 scan:** the gland is clearly seen, because trapping is intact (Fig. 4.11). The normal-looking pertechnetate scan with no activity on the delayed iodine scan, in a child with high TSH, is the classic pattern.
- **Early vs late uptake:** with defective organification (congenital defect, antithyroid drugs, Hashimoto thyroiditis), the **4–6-h uptake may be much higher than the 24-h uptake**, from avid trapping followed by washout.



• **Fig. 4.11** Congenital Organification Defect. This infant was clinically hypothyroid and had a thyroid-stimulating hormone concentration in excess of 400 mU/mL; a 24-hour iodine-123 scan showed no thyroid activity. This technetium-99m pertechnetate scan clearly shows the thyroid to be present and trapping. Normal activity in the mouth from salivary glands is seen superiorly.

Fig. 4.11. MET 7e, p. 96.

Related material: how the books assess thyroid function

- Thyroid **dysfunction is diagnosed by serum thyroid hormone and TSH**, not by radioiodine uptake. Uptake and scans are used to find the cause and plan therapy.
- Early and delayed uptake values and paired pertechnetate/delayed-iodine imaging already reveal an organification defect, as described above.

Pearls

- Perchlorate **blocks trapping** (competitive monovalent anion); it does not block organification.
- Organification defect = **gland seen on Tc-99m or early I-123, absent on 24-h radioiodine**.
- About 15% of congenital hypothyroidism is due to organification defects.

Sources

- MET 7e, ch. 4 "Thyroid, Parathyroid, and Salivary Glands", §"Radioiodine Uptake Test" (early vs 24-h uptake), p. 87; §"Congenital Organification Defects", p. 96, Fig. 4.11; Pearls, p. 114; §"Radioiodine Uptake Test" (diagnosis by serum tests), p. 86.
- REQ 5e, ch. 8 "Endocrine System", §"Thyroid Anatomy and Physiology", e-book PDF p. 462 (second book: perchlorate as a competitive monovalent-anion blocker of trapping).

[1×] F1-03 • 5 marks

What is rhTSH? Discuss the approved indications of its use. [3+2]

Asked in: Dec 2021 Paper II Q2a

What is rhTSH?

- **Synthetic recombinant human TSH (rhTSH; Thyrogen):** exogenous TSH that raises circulating TSH, so that normal or neoplastic thyroid tissue takes up radioiodine, **without stopping thyroid hormone**.
- **Why it is needed:** whole-body scans and RAI therapy need **TSH >30 mIU/mL**. Withdrawing hormone takes **4–6 weeks** (T4) and makes the patient hypothyroid; T3 can bridge but must stop 2 weeks before.
- **Regimen:** **0.9 mg intramuscularly on 2 consecutive days**. Radioiodine is given **24 h after the second dose** (day 3). Imaging follows on **day 4 for I-123** and **day 5 for I-131** (48–72 h).
- **Diagnostic activities with rhTSH:** I-123 2–4 mCi (74–148 MBq); I-131 4 mCi (148 MBq).

- **Physiological difference:** hypothyroidism lowers GFR and radioiodine clearance, but rhTSH does not affect GFR. A larger RAI activity is therefore given to match the radioiodine exposure of the withdrawal method.

Approved and accepted uses

- **Preparation for I-131 remnant ablation** after thyroidectomy: rhTSH stimulation is **FDA approved for this**, and it enhances uptake in postsurgical remnants.
- **Not approved for treating functioning metastases**, or recurrent or metastatic foci before I-131 therapy.
- **Diagnostic follow-up of DTC:** commonly used **in place of hormone withdrawal** to enhance radioiodine imaging for **recurrent thyroid cancer**, and for **stimulated serum thyroglobulin** (baseline and 6–12-monthly Tg "in the hypothyroid state or after rhTSH").
- **When withdrawal is unsuitable:** if postsurgical replacement is clinically necessary, or if TSH ≥ 30 mIU/mL cannot be reached by withholding replacement. Hypothyroid symptoms can be debilitating, particularly with comorbidities.
- **Off-label, benign disease:** not FDA approved for therapy of hyperthyroidism, but used **off-label in nontoxic nodular goiter** to maximise uptake. Pretreatment can improve success in **large goiters or low 24-h uptake**.

Table F1-03.1. rhTSH vs thyroid hormone withdrawal

Feature	Hormone withdrawal	rhTSH (Thyrogen)
Time to TSH >30	4–6 weeks off T4 (T3 stopped 2 weeks before)	0.9 mg IM on 2 consecutive days; RAI on day 3
Hypothyroid symptoms	Yes, may be debilitating	Avoided; patient stays on hormone
GFR / RAI clearance	Reduced	Unchanged, so a larger RAI activity is used
Remnant ablation	Used	FDA approved
Treatment of metastases	Used	Not approved

Current guideline (beyond the textbook)

- **ATA · 2025 Management Guidelines for Adult Patients with Differentiated Thyroid Cancer (executive summary, Thyroid 2025;35:1214–1220).** The textbook predates this.
- **Recombinant TSH is now preferred over thyroid hormone withdrawal** for RAI.

Pearls

- **0.9 mg IM $\times$ 2 days $\rightarrow$ RAI on day 3;** image on day 4 (I-123) or day 5 (I-131).
- FDA approved for **remnant ablation**, not for **treating metastases**.
- Normal GFR on rhTSH speeds RAI clearance, so a higher activity is given.
- Off-label: nontoxic multinodular goiter.

Sources

- MET 7e, ch. 4 "Thyroid, Parathyroid, and Salivary Glands", §"Whole Body Scan Technique", p. 98; Box 4.5, p. 104; §"Nontoxic Multinodular Goiter", p. 106; Box 4.6, p. 109; Pearls, p. 114.
- REQ 5e, ch. 8 "Endocrine System", §"Postthyroidectomy Scan Preparation" and §"Subsequent Follow-Up Whole-Body Thyroid Cancer Scans", e-book PDF p. 512; Box 8.7, p. 516 (second book: exact rhTSH regimen, activities and GFR effect).

F2 Hyperthyroidism, Graves' disease & thyroiditis

[4x+] F2-01 • 10 marks

Graves' disease — management (adult & paediatric)

- › Management of patients with Graves' disease. [10] — Dec 2021 • Paper III • Q10
- › Discuss the different management options of Graves's disease. Describe the role of radioactive iodine in paediatric patients with Graves's disease. [10] — Dec 2022 • Paper III • Q9
- › Discuss the different treatment options for a 25-year-old lady with Graves' disease. Discuss the advantages and disadvantages of each treatment option in her case. [6+4] — Dec 2023 • Paper III • Q4
- › Discuss the different management options in paediatric patients with Graves' disease. [10] — Dec 2024 • Paper III • Q2

Asked in: Dec 2021 Paper III Q10 • Dec 2022 Paper III Q9 • Dec 2023 Paper III Q4 • Dec 2024 Paper III Q2

Establish the diagnosis first

- **Graves disease** causes about 75% of hyperthyroidism. A **TSH-receptor antibody stimulates** the follicular cells, so function is autonomous of TSH feedback.
- Biochemistry: **elevated free T4/T3 with suppressed TSH** (<0.1 mU/L is diagnostic of thyrotoxicosis).
- **Radioiodine uptake** is elevated, usually **45%–80% at 24 h**. The scan shows a diffusely enlarged gland with a high thyroid-to-background ratio.
- The uptake test is needed to **exclude causes unsuitable for I-131** (silent/painless thyroiditis, with low uptake) and to **gauge the dose**.

Management options

- Three basic approaches: **(1) antithyroid drugs** (thioamides: propylthiouracil, methimazole); **(2) I-131 therapy**; **(3) surgery**. **β -blockers** control symptoms alongside any of them.

Table F2-01.1. Treatment options for Graves disease

Option	How it works / role	Advantages	Disadvantages
Antithyroid drugs (PTU, methimazole) $\pm$ β -blocker	Block organification; often first line; given 6–12 months or longer	Renders the patient euthyroid and gives time to decide on definitive therapy; no radiation	Adverse effects in up to 50% (liver dysfunction, agranulocytosis); often fails to control disease or induce lasting remission; full effect only after the $\sim$ 1-month hormone store is used up
I-131	Definitive treatment of choice in adults without contraindications; ideal when hyperthyroidism has medical complications or other treatments failed	Single oral dose; safe over decades (no proven rise in second cancers, infertility or congenital defects); $<10\%$ need retreatment	Hypothyroidism almost inevitable (lifelong T4); effect takes 3–6 months; may worsen ophthalmopathy; contraindicated in pregnancy and breastfeeding
Thyroidectomy	Uncommon; for very large goiters (>80 g, where I-131 at usual activities is less effective), cosmetic reasons or airway compression	Removes the goiter; relieves mass effect on the airway	Surgical complication risk (higher in young children)

Radioiodine therapy in detail

- **Patient preparation:**
 - Antithyroid drugs may be given first to deplete hormone stores, especially in **older and cardiac patients**, to reduce the risk of thyroid storm. **Stop 3–5 days before** I-131; they may be **resumed 2–3 days after** without affecting the result.
 - **β -blockers need not be stopped:** they do not affect thyroid function.
 - **NPO 2–4 h before** (preferably from midnight) and **no food or drink for 2 h after**.
 - **Pregnancy test ≤ 72 h before treatment; stop breastfeeding** (may resume only after a future birth); **avoid pregnancy for 6 months to 1 year**.
- **Contraindications** (MET Box 4.4): **pregnancy (absolute)**; continued breastfeeding; coexisting in situ or suspected thyroid cancer; inability to comply with radiation-safety guidelines. Use with informed caution if pregnancy is planned

within 4–6 months.

- **Activity:**

- **Fixed empiric 10–15 mCi (370–555 MBq)** for diffuse toxic goiter.
- **Calculated 80–200 µCi (2.96–7.4 MBq) per gram** of thyroid, from gland mass and 24-h uptake. Use higher values for large glands, nodularity, **rapid turnover (4-h > 24-h uptake)** or when rapid control is needed.
- "High-dose" therapy aiming at hypothyroidism is now the norm; low-dose therapy is rarely used. Calculated and fixed doses give similar success.

- **Course after therapy:**

- First week: sore throat, dysphagia and transient worsening of hyperthyroid symptoms.
- Symptoms improve after **3–4 weeks**; the gland shrinks within a month.
- **Hypothyroidism usually by 2–3 months**: start levothyroxine. Check thyroid function at **1 month**.
- **Repeat dose** if still hyperthyroid after **3–4 months**.

- **Release** (NRC rules in MET): dose rate at 1 m ≤ 7 mrem/h (**0.07 mSv/h**), or dose ≤ 33 mCi (**1.2 GBq**), or calculated dose to others ≤ 500 mrem (5 mSv). Give **5–7 days** of ALARA precautions.

- **Ophthalmopathy**: radiation-induced hypothyroidism raises the risk of exacerbation, especially in **smokers**. Minimise it with **concurrent oral prednisone** or prompt hormone replacement. Patients without orbitopathy rarely develop it.

Worked example — Calculated I-131 activity for Graves disease (REQ Box 8.6 values)

- Gland weight 60 g; 24-h uptake 80%; desired retained activity 100 µCi/g (intended to deliver 8000–10,000 rad to the thyroid).
- Required activity = $(60 \text{ g} \times 100 \text{ µCi/g}) / 0.80 = 7500 \text{ µCi} = 7.5 \text{ mCi (277.5 MBq)}$.

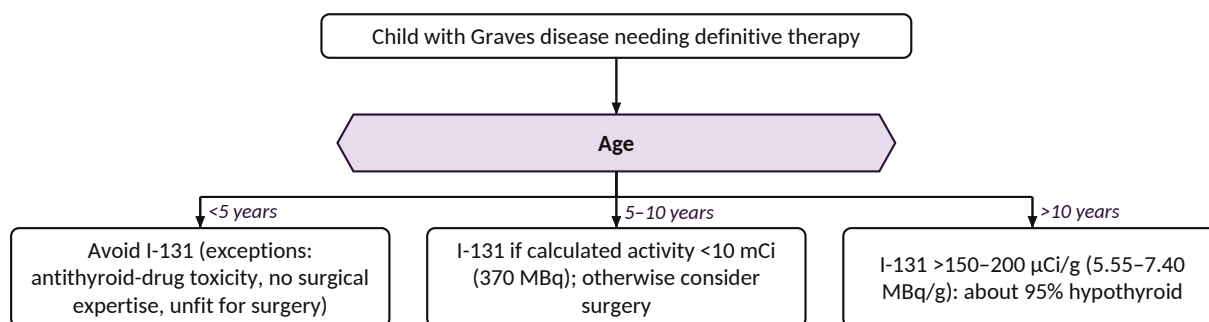
Case: a 25-year-old woman with Graves disease

- **Antithyroid drugs**: avoid radiation. But they often fail to induce lasting remission, therapy runs 6–12 months, and up to half have side effects (agranulocytosis, liver injury).
- **I-131**: definitive, single outpatient dose, safe for her future children. But she will need **lifelong T4**, must **not be pregnant or breastfeeding**, must **avoid conception for 6 months to 1 year**, and her eyes may worsen (higher risk if she smokes; prednisone cover).
- **Surgery**: suits a **very large goiter** or local compression; otherwise rarely chosen for uncomplicated disease.

Graves disease in children

- Graves disease is the commonest cause of paediatric hyperthyroidism.
- **Antithyroid drugs** give lasting remission in only a small minority. **Up to 80%** of children eventually need I-131.
- **Surgery** carries higher complication risks in young children.
- **Goal of I-131**: induce hypothyroidism in **one dose**. Low activities cause recurrence and leave partly irradiated tissue at increased risk of neoplasia.
- **Calculated** (not fixed) activities are preferred, and the activity must **not be arbitrarily reduced** in a child.
- Some practitioners restrict I-131 to post-pubertal patients or those over 20 years because of perceived cancer risk.
- There is **no increase in spontaneous abortion or congenital anomalies** in offspring. Thyroid storm occurs in $<0.1\%$.

Flowchart F2-01.1. Choosing I-131 by age in paediatric Graves disease (MET p. 106)



Current guideline (beyond the textbook)

- **ATA • 2016 Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis (Thyroid 2016).** The textbook predates this.
- **Recommendation 3** (strong, moderate-quality evidence): overt Graves hyperthyroidism should be treated with **RAI, ATDs or thyroidectomy**.
- **Factors favouring RAI:** a woman planning pregnancy **more than 6 months after treatment**; comorbidity raising surgical risk; prior neck surgery or irradiation; ATD failure or contraindication.
- **Factors favouring ATDs:** high likelihood of remission (mild disease, small goiter, negative or low-titre TRAb); pregnancy; moderate-to-severe active orbitopathy.
- **Factors favouring surgery:** compressive or large goiters (**≥80 g**); documented or suspected malignancy; large non-functioning nodules; coexisting hyperparathyroidism needing surgery.
- **Definite contraindications to RAI:** pregnancy, lactation, coexisting or suspected thyroid cancer.

Pearls

- I-131 is the **definitive treatment of choice** for adult Graves disease; expect hypothyroidism by **2–3 months**.
- **Fixed 10–15 mCi or 80–200 µCi/g**; give more for rapid turnover (4-h > 24-h uptake).
- Stop ATDs **3–5 days before**; restart **2–3 days after**; β-blockers continue.
- **Prednisone cover** for active orbitopathy, especially in smokers.
- Children: avoid I-131 under **5 years**; give >150–200 µCi/g over 10 years.

Sources

- MET 7e, ch. 4 "Thyroid, Parathyroid, and Salivary Glands", §"Iodine-131 Therapy in Hyperthyroidism", §"Patient Preparation and Post-Treatment Expectations", pp. 103–105, Box 4.5, p. 104; §"Diffuse Toxic Goiter", pp. 105–106; §"Iodine-131 Therapy of Hyperthyroidism in Children", p. 106; Box 4.4, p. 100; §"Early Side Effects and Late Sequelae", p. 110.
- REQ 5e, ch. 8 "Endocrine System", §"Thyrotoxicosis—Hyperthyroidism" and §"Thyroid Anatomy and Physiology" (1-month hormone store), p. 462; §"Graves disease", e-book PDF pp. 484–485; §"Radioiodine I-131 Therapy of Thyrotoxicosis", §"Iodine-131 Dose Selection for Graves", pp. 503–506; Box 8.6, pp. 515–516 (second book: TSH cut-off, uptake range, ATD duration and toxicity, worked dose calculation).

[1×] F2-02 • 5 marks

Clinical activity scores in the management of Graves' ophthalmopathy. [5]

Asked in: Jun 2021 Paper III Q9b

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "clinical activity score", "CAS", "ophthalmopathy", "orbitopathy", "exophthalmos", "EUGOGO". Checked MET ch. 4 and REQ ch. 8.
- The Clinical Activity Score is not described in any of the five books. Related book material follows, then the guideline content in the amber box.
- Ophthalmopathy, orbitopathy and exophthalmos occur only as features of Graves disease and of its I-131 therapy (MET pp. 104, 110; REQ ch. 8); 'CAS' hits are ordinary words.

Related material in the books: radioiodine and Graves orbitopathy

- **Exophthalmos and pretibial oedema** are classic signs of Graves disease.
- Orbitopathy is **not controlled by antithyroid drugs or I-131**, and it **may worsen or develop after I-131**. This belongs in the consent.
- **Mechanism of worsening:** radiation-induced **hypothyroidism** confers an increased risk of exacerbation, **especially in smokers**.
- **Prevention: concurrent oral prednisone (corticosteroids)** with I-131 or **prompt thyroid hormone replacement**. Patients **without orbitopathy are unlikely to develop it** after radioiodine.
- **Somatostatin-receptor imaging:** In-111 pentetreotide accumulates in Graves disease and **Graves ophthalmopathy**, an autoimmune source of positive (false-positive for tumour) studies.

Current guideline (beyond the textbook)

- **EUGOGO · The 2021 European Group on Graves' Orbitopathy clinical practice guidelines for the medical management of Graves' orbitopathy (Eur J Endocrinol 2021;185:G43–G67).** The textbooks do not cover this.
- **CAS: 7 items, 1 point each:** spontaneous retrobulbar pain; pain on attempted upward or downward gaze; redness of the eyelids; redness of the conjunctiva; swelling of the caruncle or plica; swelling of the eyelids; chemosis (conjunctival swelling).
- **GO is active if CAS $\geq 3/7$.**
- **Severity:** mild (minor impact on daily life); moderate-to-severe (no threat to sight but enough impact, e.g. lid retraction ≥ 2 mm, exophthalmos ≥ 3 mm above normal); sight-threatening (dysthyroid optic neuropathy and/or corneal breakdown).
- **Treatment by activity and severity:**
 - Mild: local measures and risk-factor control; **selenium for 6 months** in mild active GO of recent onset.
 - Moderate-to-severe active: **IV methylprednisolone 0.5 g weekly $\times$ 6, then 0.25 g weekly $\times$ 6 (cumulative 4.5 g) with mycophenolate.**
 - Optic neuropathy: high-dose IV methylprednisolone, then urgent orbital decompression if the response is poor in 1–2 weeks.
- **RAI prophylaxis:** oral prednisone/prednisolone for patients at risk; **0.3–0.5 mg/kg tapered over 3 months** (high risk) or **0.1–0.2 mg/kg over 6 weeks** (low risk).

Pearls

- CAS = **7 inflammatory signs**; $\geq 3/7$ = **active** (amenable to immunosuppression).
- I-131 can **worsen GO**, especially in smokers and with uncorrected hypothyroidism: give **prednisone** and **prompt T4**.
- Severity (mild / moderate-to-severe / sight-threatening) and activity are graded separately.

Sources

- MET 7e, ch. 4 "Thyroid, Parathyroid, and Salivary Glands", Box 4.5, p. 104; §"Early Side Effects and Late Sequelae of Iodine-131 Therapy", p. 110; ch. 10 "Non-PET Neoplasm Imaging and Radionuclide Therapy", Table 10.2 (somatostatin-receptor imaging), p. 320.
- REQ 5e, ch. 8 "Endocrine System", §"Graves disease", e-book PDF p. 485; §"Radioiodine I-131 Therapy of Thyrotoxicosis", p. 503 (second book: orbitopathy not controlled by ATD/I-131; corticosteroid cover).

[1×] F2-03 • 5 marks

Define thyroid storm and enumerate its clinical management. [2+3]

Asked in: Jun 2023 Paper III Q4b

NOT COVERED IN SOURCE

- Searched MET 7e, REQ 5e, SAHA 7e, CSP 4e and IAEA 2014, full text and index pages, for "thyroid storm", "thyrotoxic crisis", "storm", "Burch-Wartofsky". Checked MET ch. 4 and REQ ch. 8.
- The books mention thyroid storm only as a rare complication of I-131 therapy. A formal definition, diagnostic criteria and a management protocol are not given. Book material first, then the guideline in the amber box.

Definition and mechanism (book material)

- **Thyroid storm:** a rare, potentially **life-threatening** exacerbation of thyrotoxicosis.
- After I-131 it results from the **sudden release of accumulated hormone** from radiation-damaged follicles.
- **Incidence after radioiodine: less than 0.1%.**
- **At-risk patients:** those in a **very toxic state**, those given **higher activities**, and **older and cardiac** patients.

Prevention and management in the radioiodine setting (book material)

- **Pretreat severely hyperthyroid patients with antithyroid drugs** to deplete stored hormone; stop 3–5 days before I-131 and resume 2–3 days after.
- **β -blockers** before and after therapy minimise the risk, and may be continued throughout.
- Established storm **may require hospitalisation and steroid therapy.**