Baylor College of Medicine

DEPARTMENT OF PEDIATRICS

Texas Children's Hospital®



# Problemas endocrinológicos comunes en oncología

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División de Diabetes y Endocrinología Pediátrica
Director de Neoplasias Endocrinas y Trastornos Tiroideos

# Declaración de conflictos de interés

El presentador declara que no tiene relaciones financieras ni conflictos de interés que declarar para esta actividad.

La presentación combina dos idiomas:

- Exposición y textos en español
- Gráficos en inglés

¿Qué porcentaje de los sobrevivientes de cáncer infantil estima que presenta al menos un trastorno endocrino?

A. Menos del 25 %

B. Del 25 al 49 %

C. Del 50 al 74 %

D. El 75 % o más

Seleccione una opción en la encuesta de Teams.

¿Qué grupo de trastornos endocrinos es el más frecuente en los sobrevivientes de cáncer infantil?

A. Trastornos tiroideos

B. Deficiencia de hormona de crecimiento

C. Trastornos reproductivos

D. Trastornos del metabolismo de la glucosa

Seleccione una opción en la encuesta de Teams.

Un sobreviviente de cáncer infantil recibió radioterapia craneo-espinal (35 Gy)  y no presenta alteraciones endocrinas cinco años después. ¿Cuál es la mejor conducta?

A. Suspender la vigilancia endocrina

B. Continuar únicamente hasta completar la pubertad

C. Reevaluar solo si reaparece el cáncer

D. Mantener vigilancia de por vida, adaptada a su riesgo

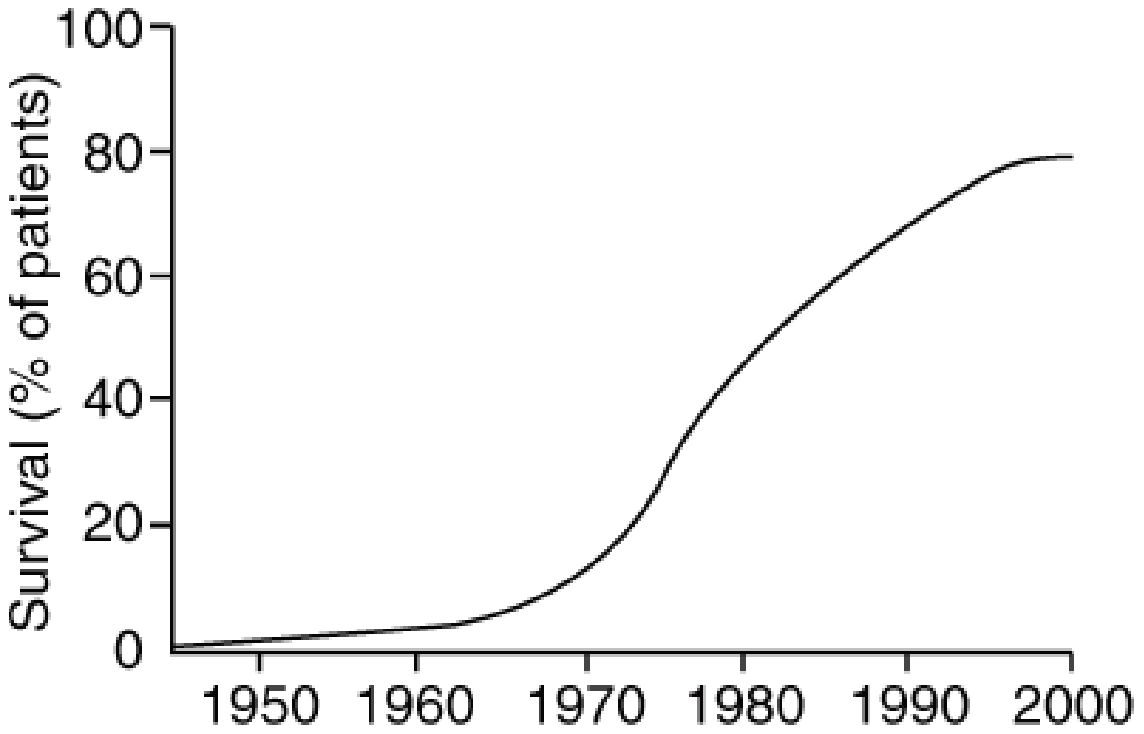
Seleccione una opción en la encuesta de Teams.

# «La cura» del cáncer pediátrico

El Dr. Donald Pinkel describió la «terapia total» para la leucemia aguda en 1962

- Quimioterapia múltiple
- Quimioterapia intratecal
- Radioterapia





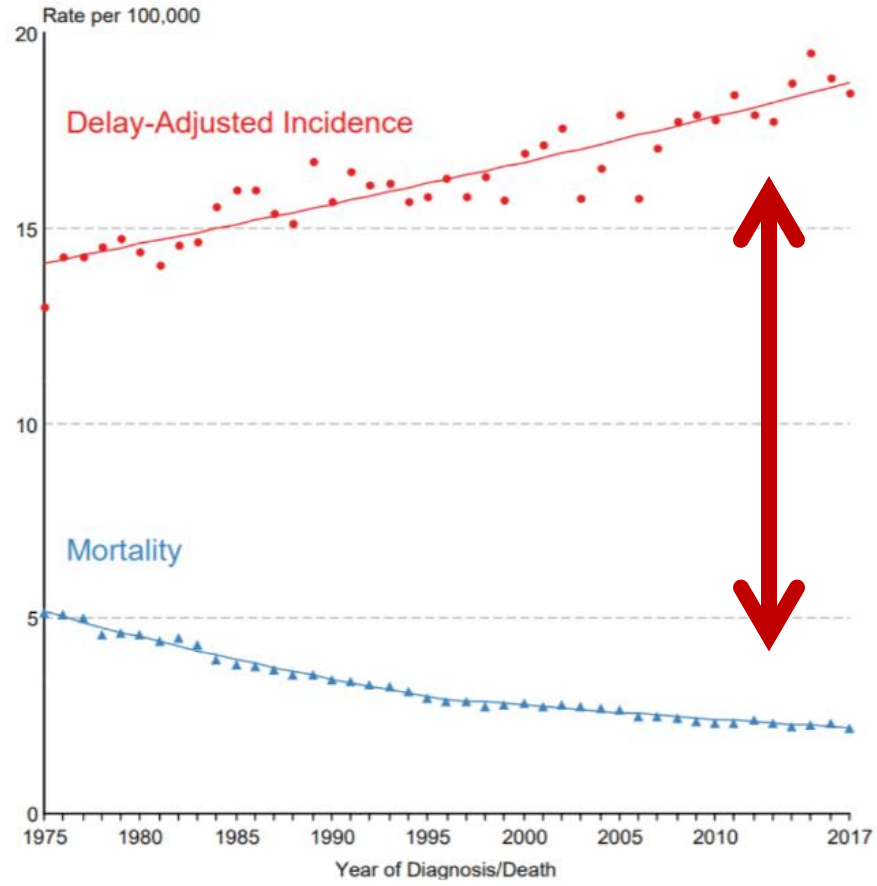

*Pinkel, D. Pediatr Res. 1971; 5, 408*

# El cáncer pediátrico va en aumento

## También aumenta el número de sobrevivientes de cáncer pediátrico (SCP)

- Cáncer pediátrico (<19 años)
  - Sobrevida a 5 años: 85 %
  - Incidencia anual: 18,7 por 100.000

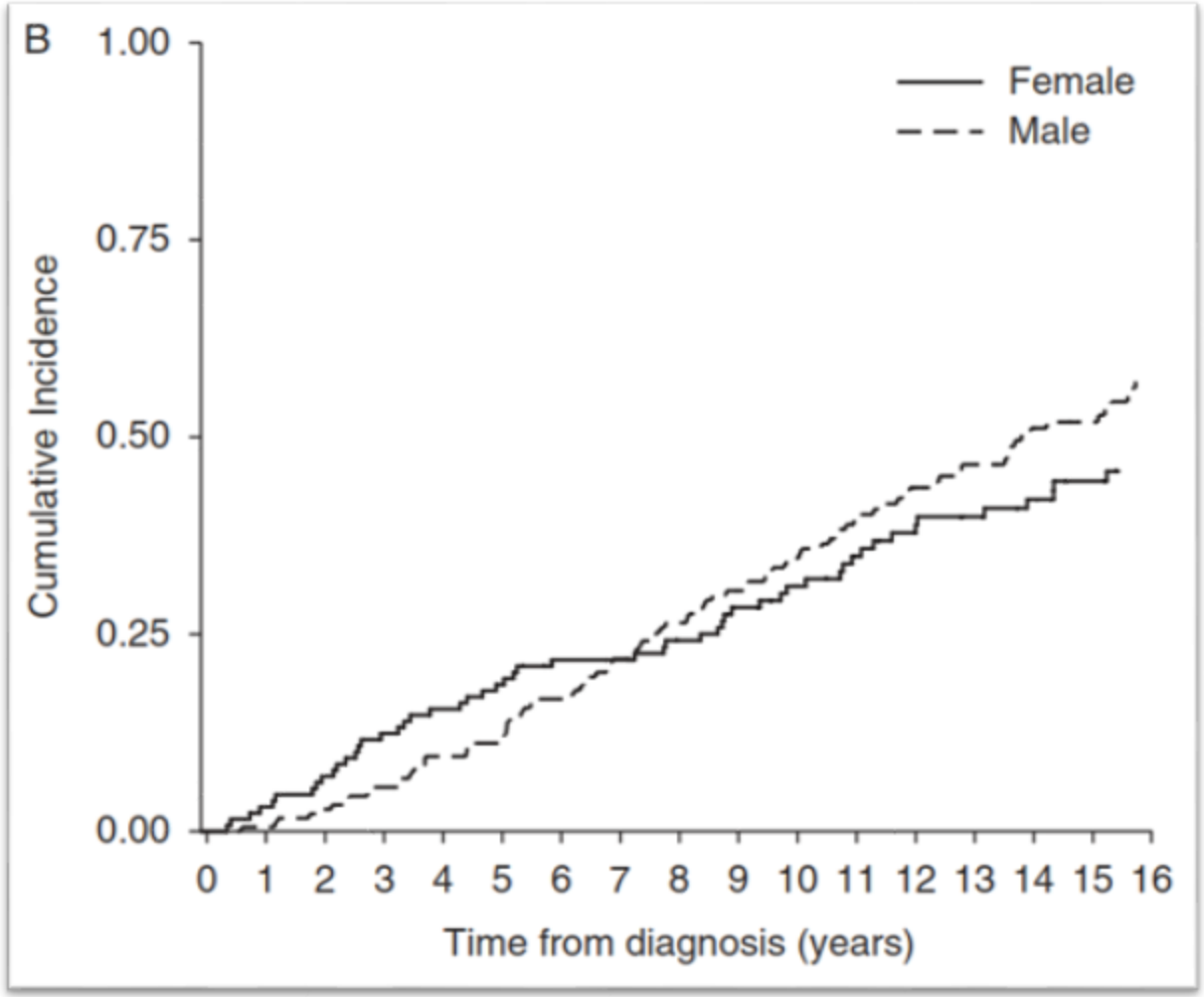
- SCP estimados para el 2020
  - 1 de cada 750 adultos
  - Medio millón de sobrevivientes






National Cancer Institute. SEER cancer statistics review 1975-2015.
Sklar, CA. et al. J Clin Endocrinol Metab. 2018;103:2761-84

# Las endocrinopatías son frecuentes en los SCP




Brignardello et al. European Journal of endocrinology. 2013;168:465-72

# Sobrevivientes de cáncer pediátrico en Latinoamérica

| País | Población | Incidencia anual | Supervivencia a 5 años (%) | SCP anuales | SCP con trastorno endocrino por habitante | Fuente |
|---|---|---|---|---|---|---|
| **Costa Rica** CR | 5.2 M | 180 | 79.0 | 142 | 1 por cada 73,239 | [A][B] |
| **Chile** CL | 19.6 M | 500 | 78.4 | 392 | 1 por cada 100,000 | [C] |
| **Argentina** AR | 46.2 M | 1,400 | 70.0 | 980 | 1 por cada 94,286 | [D] |
| **Brasil** BR | 215.3 M | 7,900 | 64.0 | 5,056 | 1 por cada 85,166 | [E] |
| **Colombia** CO | 52.1 M | 1,950 | 59.5 | 1,131 | 1 por cada 92,131 | [F] |
| **México** MX | 128.5 M | 6,000 | 56.1 | 3,366 | 1 por cada 76,352 | [A][G] |
| **Perú** PE | 34.4 M | 1,680 | 55.0 | 924 | 1 por cada 74,459 | [A] |
| **Ecuador** EC | 18.2 M | 800 | 50.0 | 400 | 1 por cada 91,000 | [A] |
| **Guatemala** GT | 18.1 M | 900 | 50.0 | 450 | 1 por cada 80,444 | [A] |

**Fuentes**

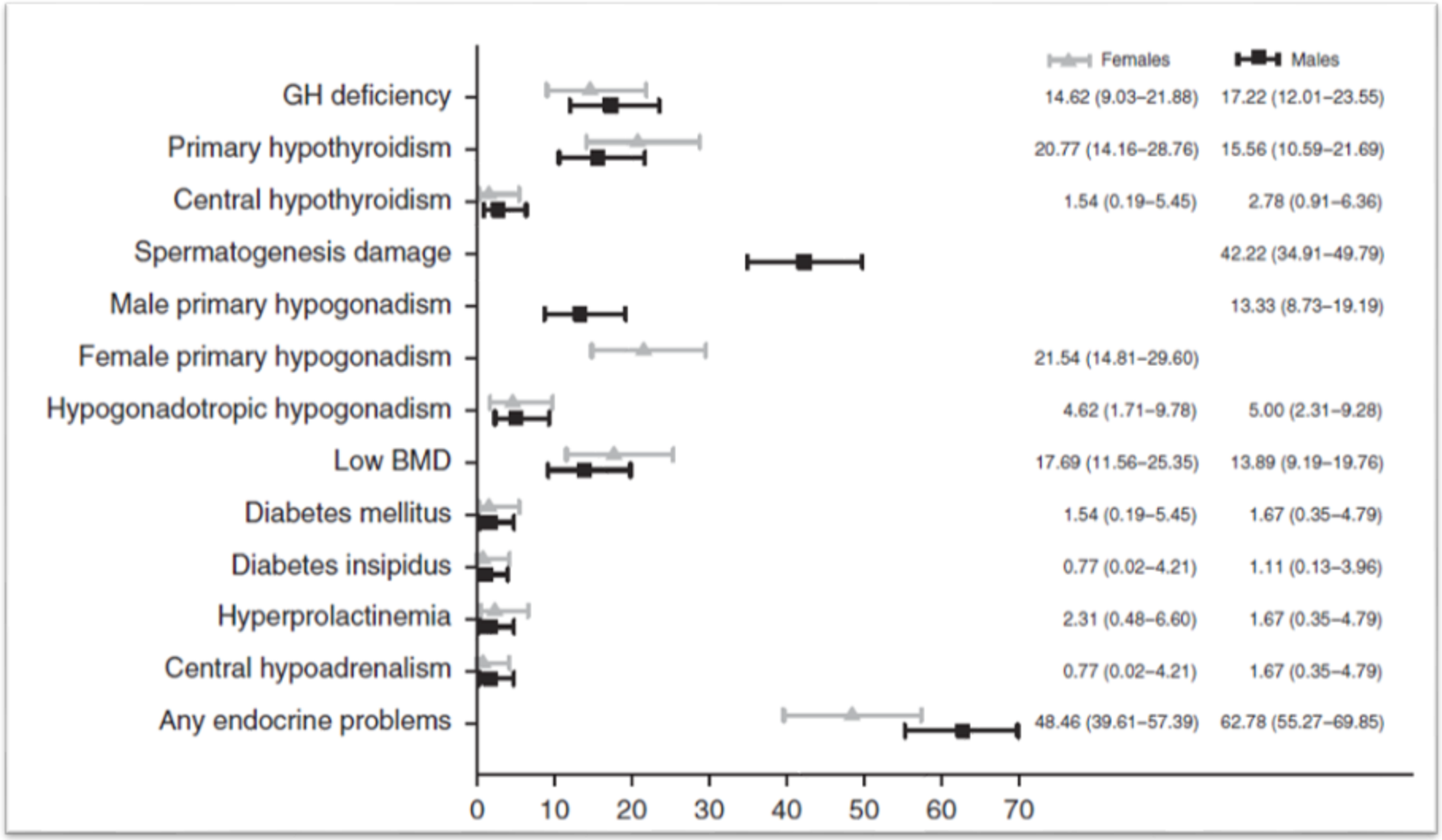
[A] OPS/OMS (PAHO/WHO): Perfiles de País sobre Cáncer Infantil — Costa Rica, México, Perú, Ecuador y Guatemala.

[B] CCSS, Costa Rica · [C] RENCI / Ministerio de Salud, Chile · [D] ROHA / Instituto Nacional del Cáncer, Argentina.

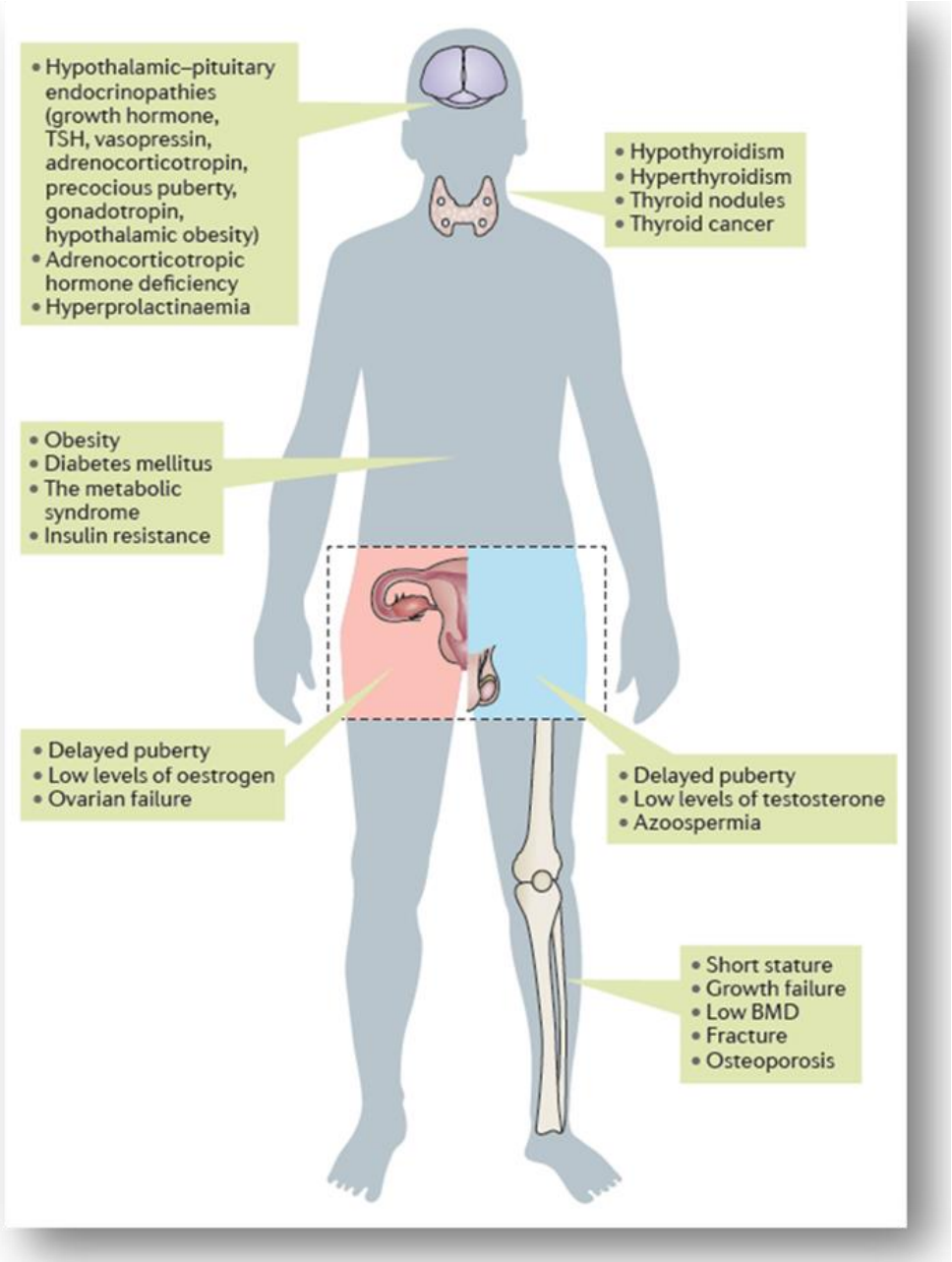
[E] INCA / Ministério da Saúde, Brasil · [F] INS / Ministerio de Salud, Colombia · [G] IMSS, México.

Nota metodológica: la columna F supone que 50% de los sobrevivientes presenta al menos un trastorno endocrino.

# Las endocrinopatías más frecuentes en los SCP




Brignardello et al. European Journal of endocrinology. 2013;168:465-72






Rose, SR. et al. Nat Rev Endo. 2016;12:319-36

# Causas de endocrinopatías en los SCP



Efectos del cáncer o del tumor



Cirugía



Quimioterapia



Radioterapia

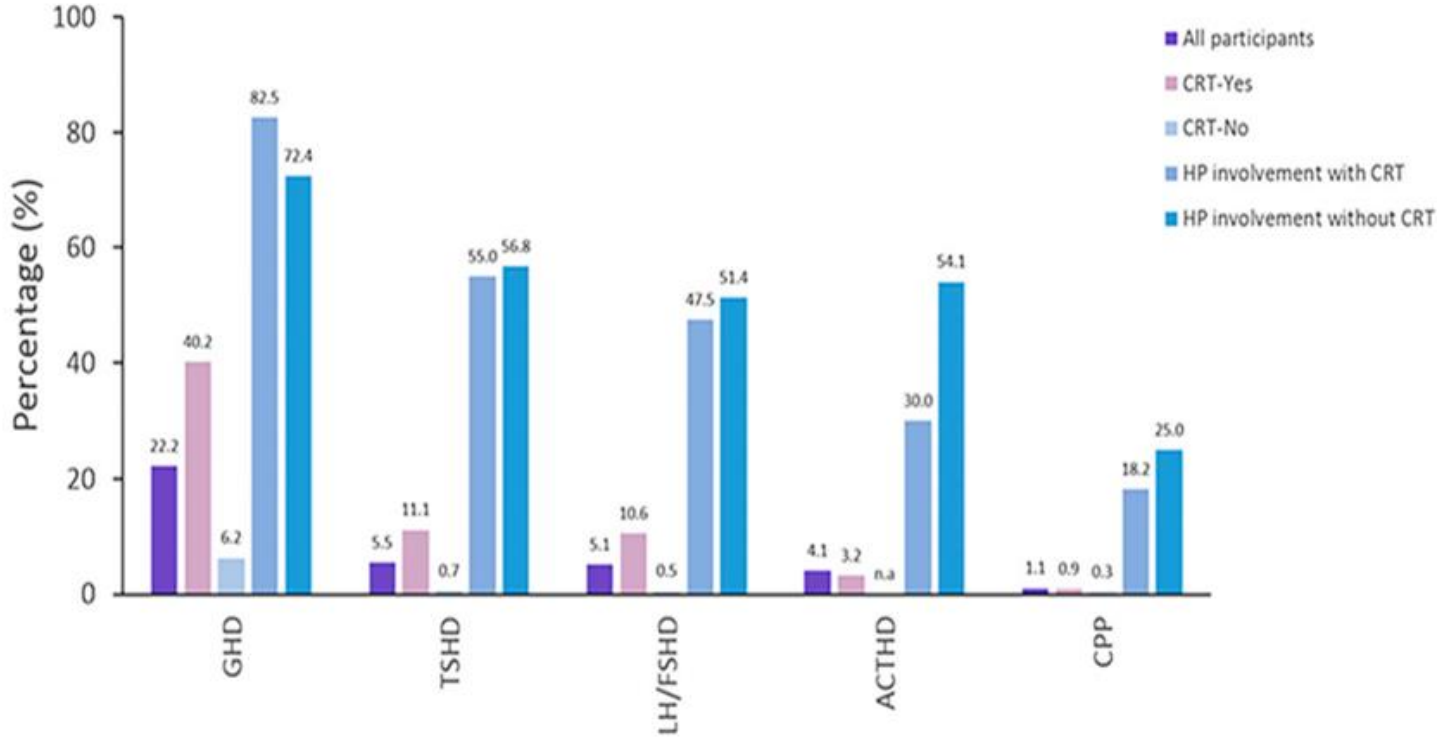


Endocrine Society. Childhood Cancer Survivors and Endocrine Gland Disruption. 2022.

# Dependen del diagnóstico y de la localización

## Tumores cerebrales

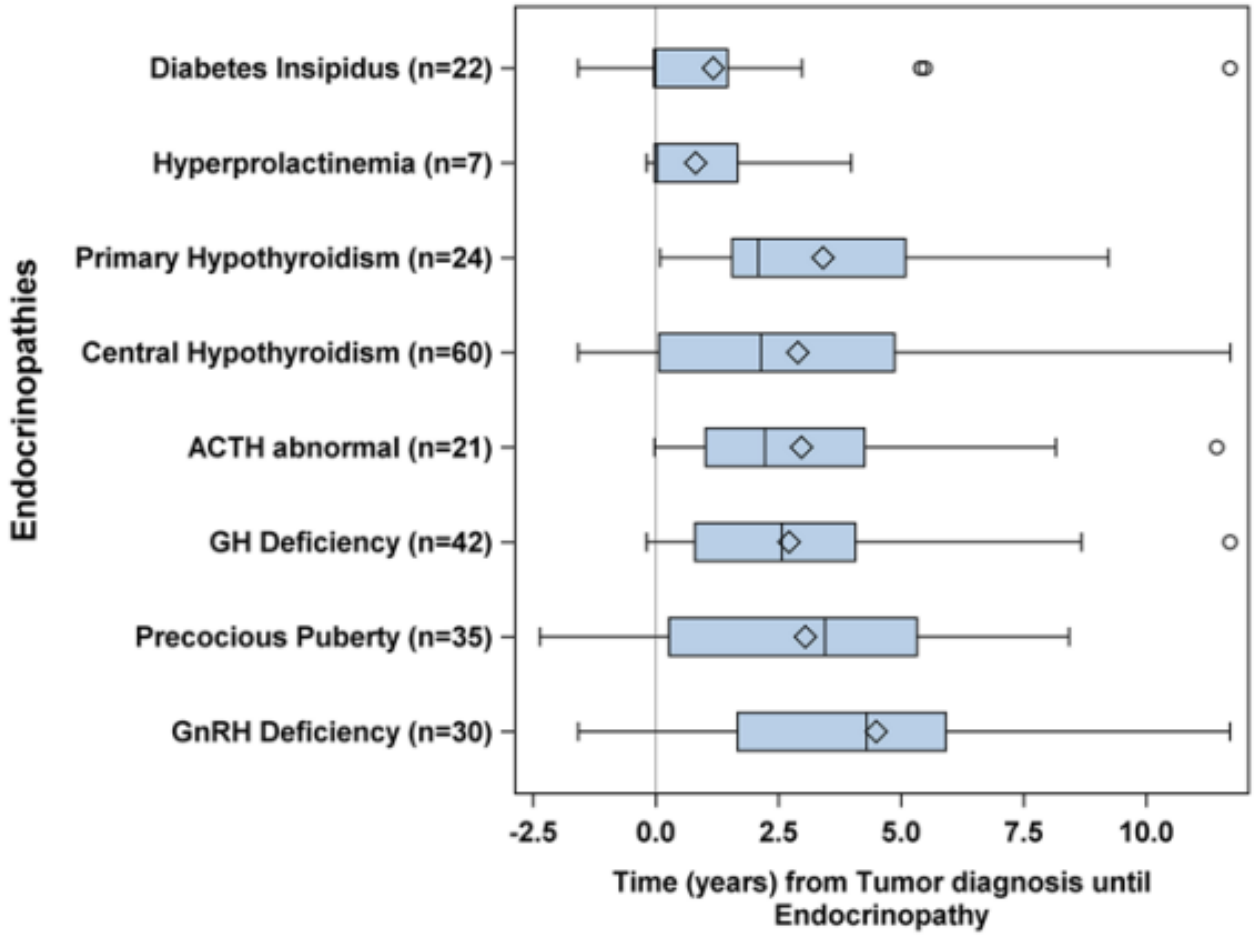
- 15 % de diagnósticos, pero con mayor riesgo de endocrinopatías
  - Conducen al diagnóstico neoplásico
  - 87 % de los craneofaringiomas al diagnóstico
  - DI puede presentarse antes de hallazgos imagenológicos
- Gliomas de la vía óptica
  - Pubertad precoz
  - Exceso de hormona de crecimiento
- Adenomas funcionantes
  - Pituitaria
  - Adrenal
- Feocromocitoma/paraganglioma






Van Iersel, L. J Clin Endocrinol Metab. 2019; 104(12)

# Aparición de endocrinopatías en tumores cerebrales



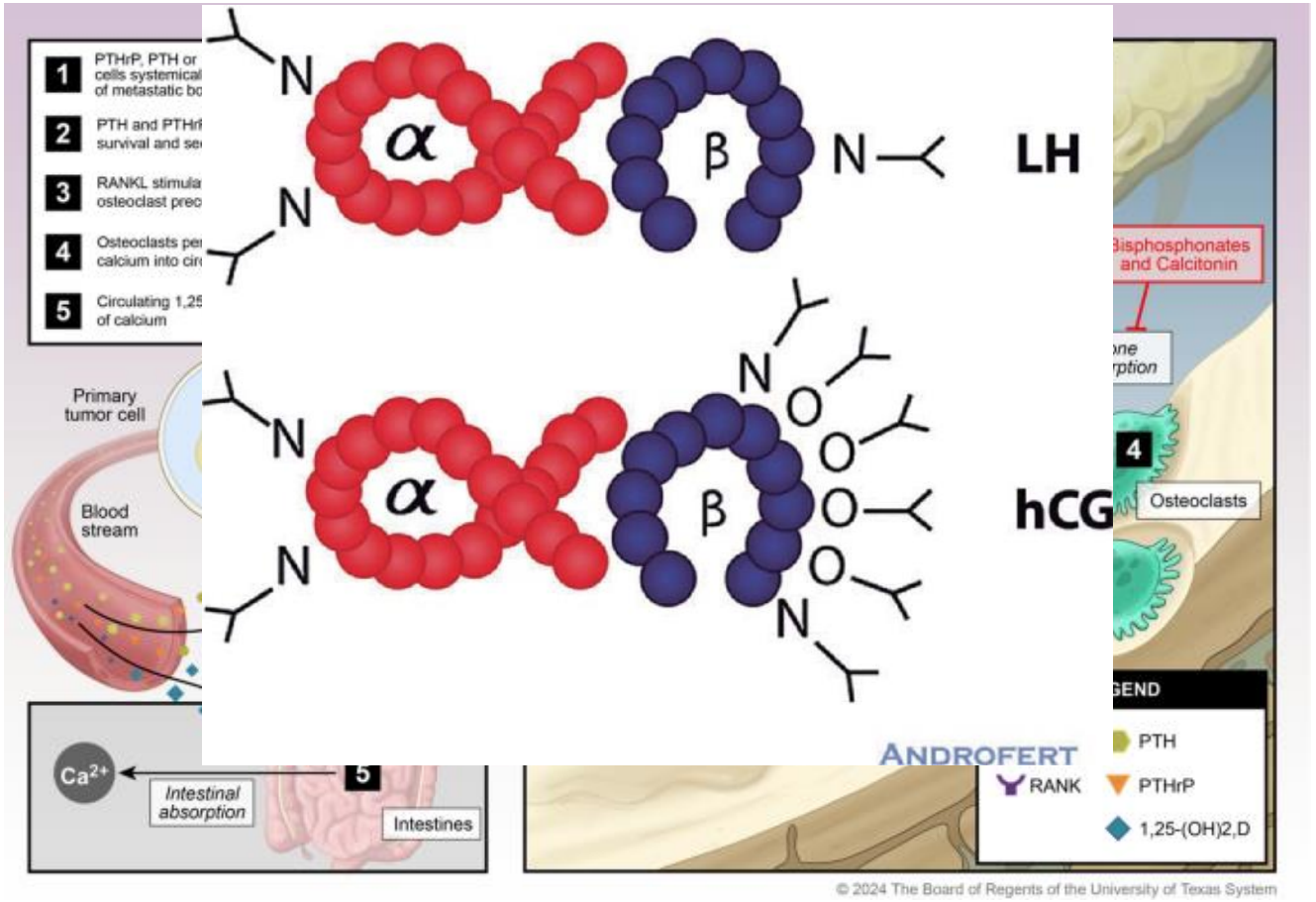



Lawson, SA., Pediatr Blood Cancer. 2019 May;66(5):e27631

# Fenómenos para-neoplásicos

- Hipercalcemia de origen maligno

- Precocidad sexual
  - hCG en tumores de células germinales
  - Testosterona en tumores de células de Leydig






Crouch, A. et al. Curr Oncol Rep. 2025;27: 871–882

# Causas de endocrinopatías en los SCP



Efectos del cáncer o del tumor



Cirugía



Quimioterapia



Radioterapia

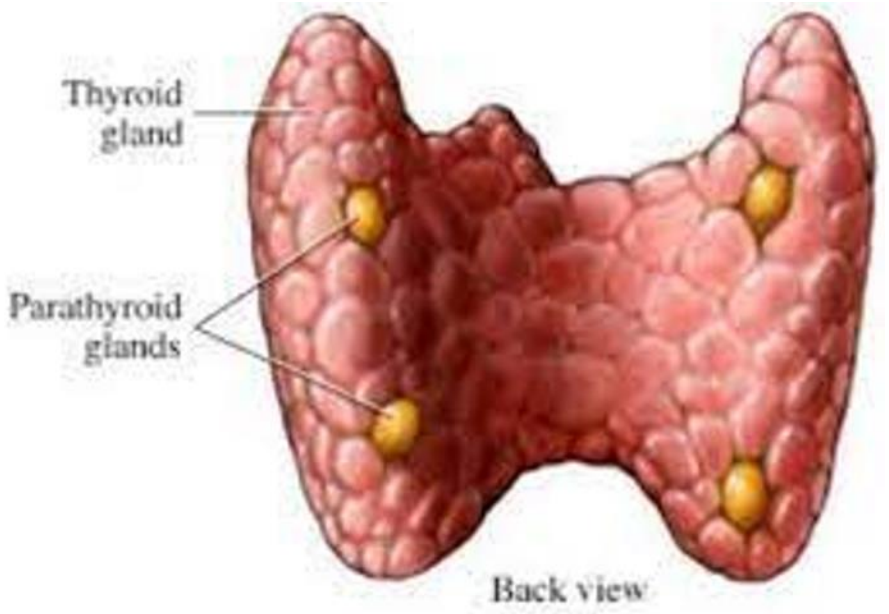


Endocrine Society. Childhood Cancer Survivors and Endocrine Gland Disruption. 2022.

# Endocrinopatías posquirúrgicas

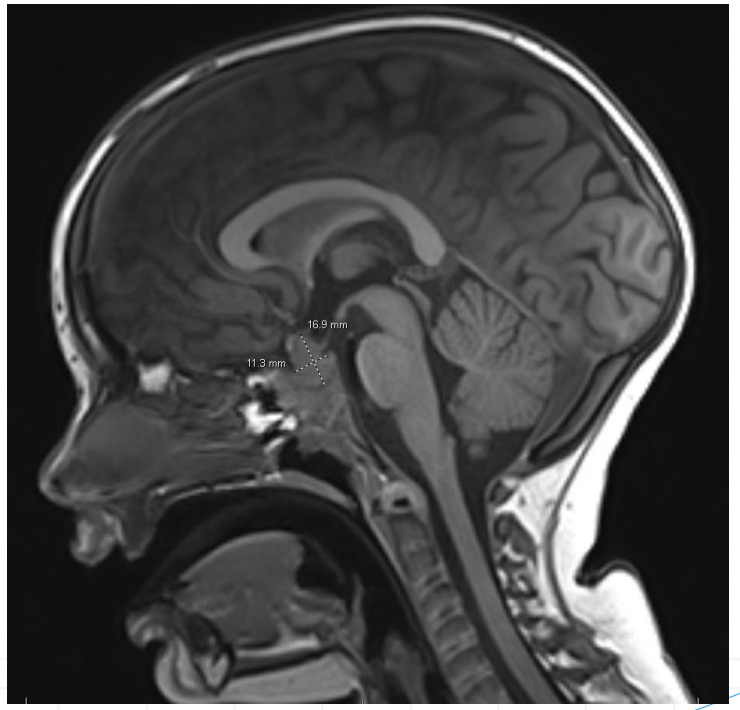
- Directos
  - Hipotiroidismo
  - Diabetes mellitus
  - Hipogonadismo

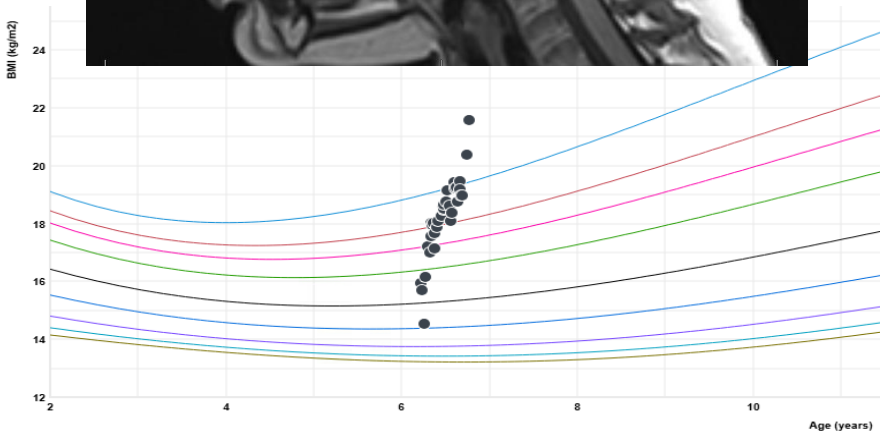
- Indirectos
  - Hypopituitarismo y/o síndrome hipotalamico, especialmente tumores selares
  - Hipoparatiroidismo en cáncer de tiroides



# Síndrome hipotalámico

- Se caracteriza por un aumento de peso intratable, múltiples anomalías endocrinas y deterioro de la memoria, déficit de atención y menor control de los impulsos, así como un mayor riesgo de trastornos cardiovasculares y metabólicos.
- Obesidad hipotalámica
  - Altera la regulación central de la saciedad, el gasto energético y la función autonómica
  - Afecta al 50 % de los pacientes con craneofaringiomas, independientemente de la sustitución hormonal hipofisaria
- Adipsia






Diabetes Obes Metab. 2024; 2:34-45.
Muller, HL. Nat Rev Dis Primers. 2022;21;8(1):24.

# Causas de endocrinopatías en los SCP



Efectos del cáncer o del tumor



Cirugía



Quimioterapia

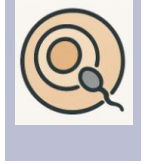


Radioterapia



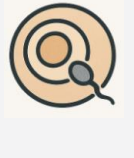
Endocrine Society. Childhood Cancer Survivors and Endocrine Gland Disruption. 2022.

# Efectos de la quimioterapia



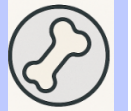
**Agentes alquilantes (CED)**

- Hipogonadismo y subfertilidad
- Osteopenia
- Deficiencia de GH: IT
- ¿Hipotiroidismo?: dosis altas



**Agentes de platino**

- **Hypogonadismo y subfertilidad**
- **Aumentariesgo de injuria for radiacion**



**Antimetabolitos**

- Crecimiento deficiente
- Osteopenia



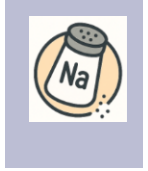
**Glucocorticoides**

- Crecimiento deficiente
- Osteopenia
- Hiperglucemia
- Necrosis avascular
- Insuficiencia suprarrenal




**PEG-Asp y 6-MP**

- Hipoglicemia
- Hiperglucemia




**Vincristina y vinblastina**

- SIADH



**Inhibidores de tirosina cinasa**

- Hipotiroidismo
- Crecimiento deficiente
- Hipoparatiroidismo
- Hipogonadismo



**Inhibidores de puntos de control inmunitario**

- Tiroiditis
- DM tipo 1
- Insuficiencia suprarrenal
- ¿Hipofisitis?

# Causas de endocrinopatías en los SCP



Efectos del cáncer o del tumor



Cirugía



Quimioterapia

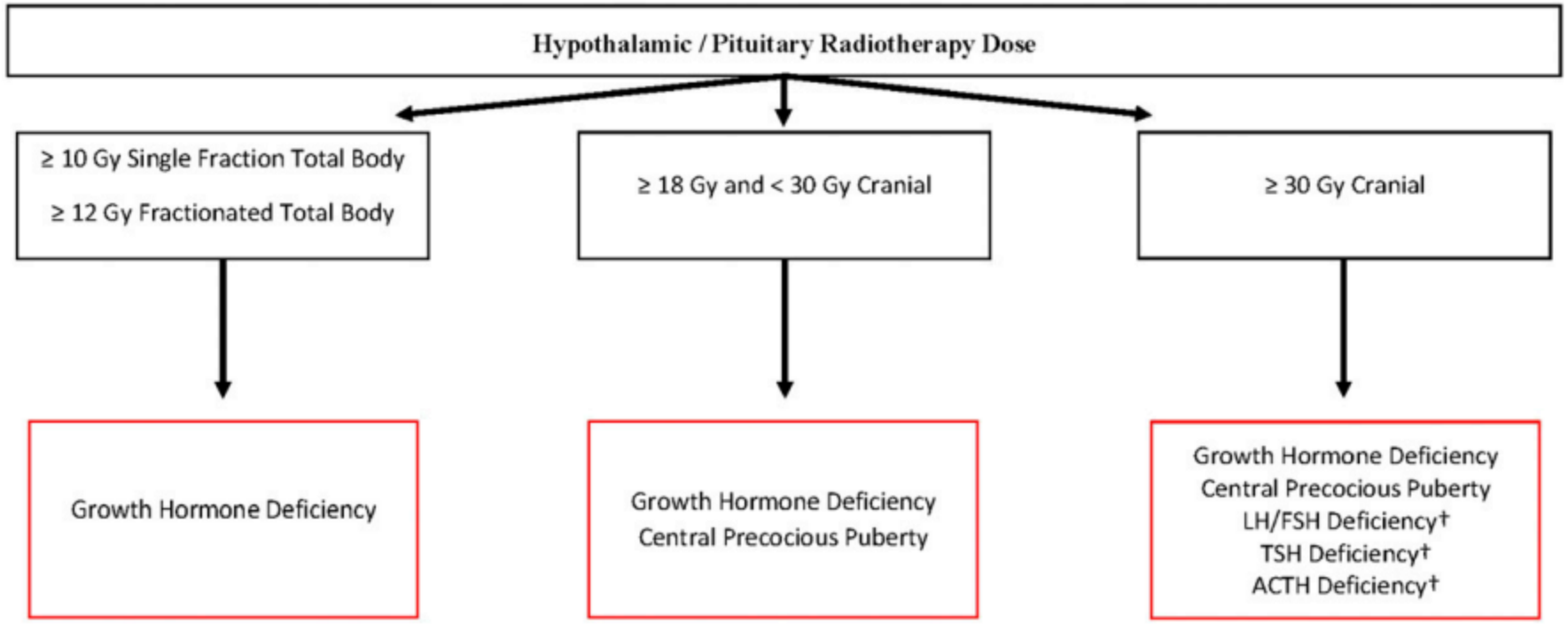


Radioterapia



Endocrine Society. Childhood Cancer Survivors and Endocrine Gland Disruption. 2022.

# Dependen de la dosis recibida

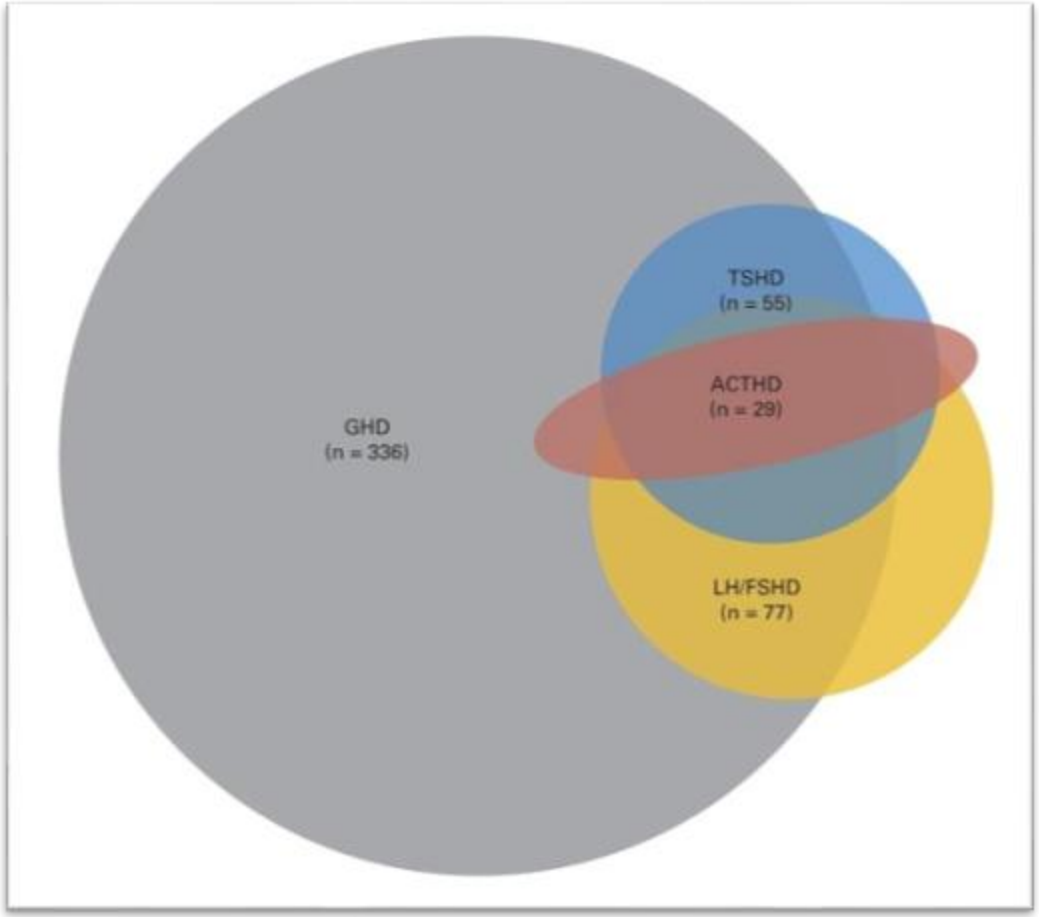



Sin deficiencia de vasopresina (AVP)



Sklar, C. J Clin Endocrinol Metab. 2018;103(8):2761-84

# Deficiencia de GH como centinela

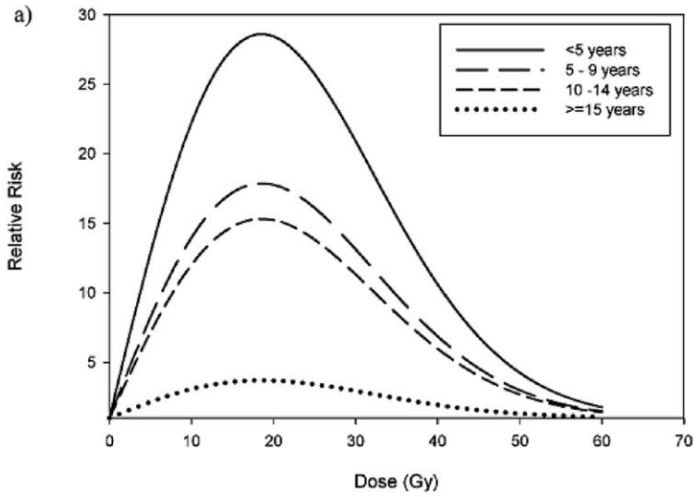


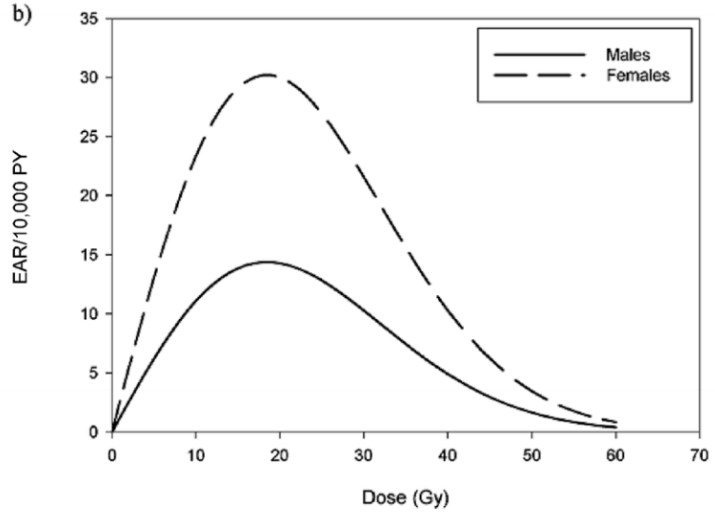

Chemaitilly W. *J Clin Oncol*. 2015;33(5):492-500

# Factores del paciente

## Más allá de la dosis

- Edad
- Sexo
- Estado puberal



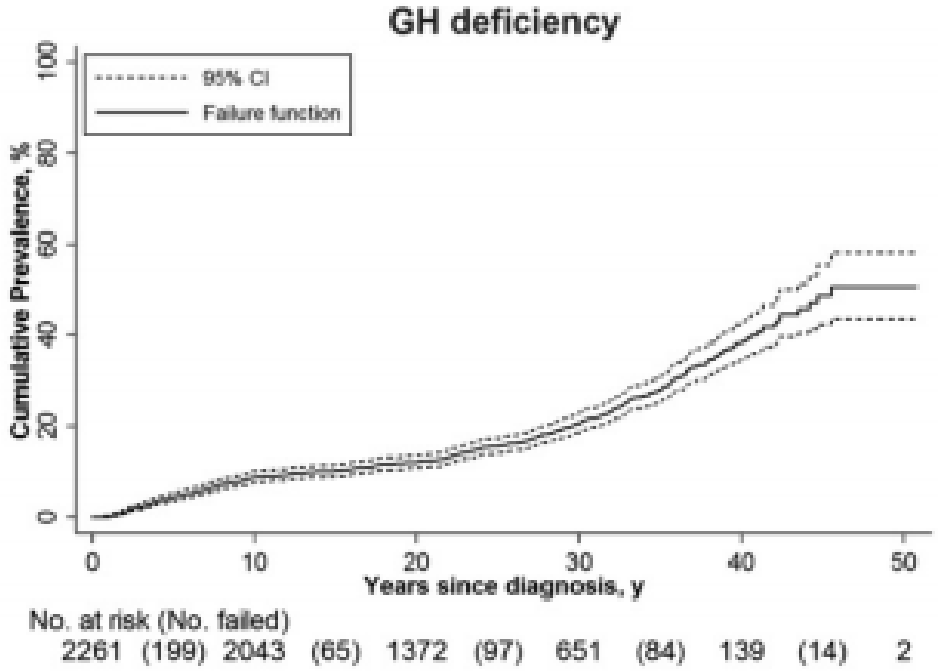

| | | | Minimally Increased Risk | Significantly Increased risk | High level of Increased risk |
|---|---|---|---|---|---|
| Radiation exposure | Ovary | Prepubertal | | < 15 Gy | ≥ 15 Gy |
| | | Pubertal | | < 10 Gy | ≥ 10 Gy |

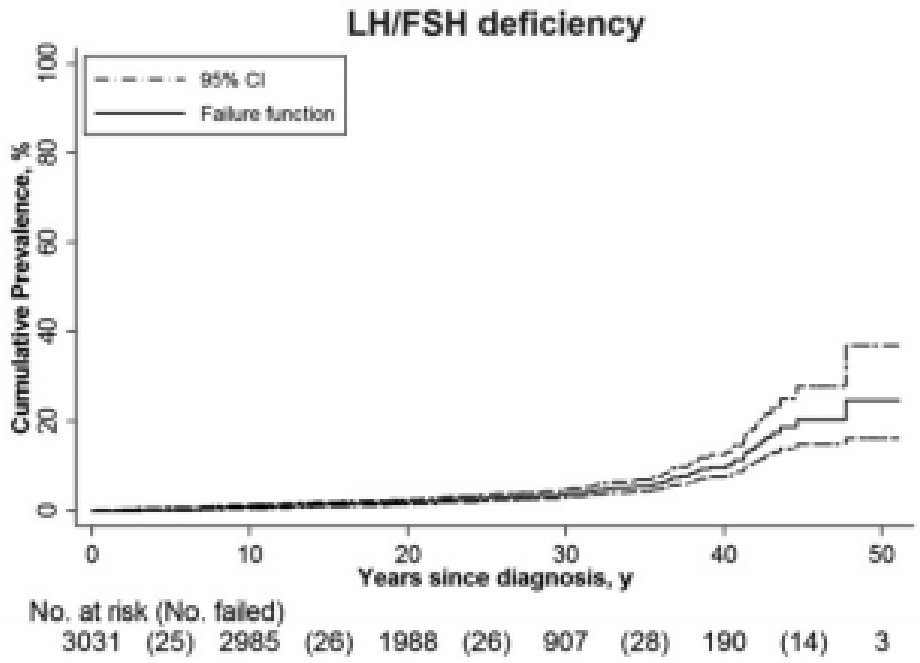


Bhatti et al. Radiat Res. 2010 Dec;174(6):741-52
Meacham, L. et al. J Adolesc Young Adult Oncol. 2020 Dec;9(6):662-666.

# Los efectos de la radiación son latentes

- Pueden presentarse incluso décadas después del tratamiento
- Requieren seguimiento de por vida






Van Hersel et al. J Clin Endocrinol Metab 104:6101–6115

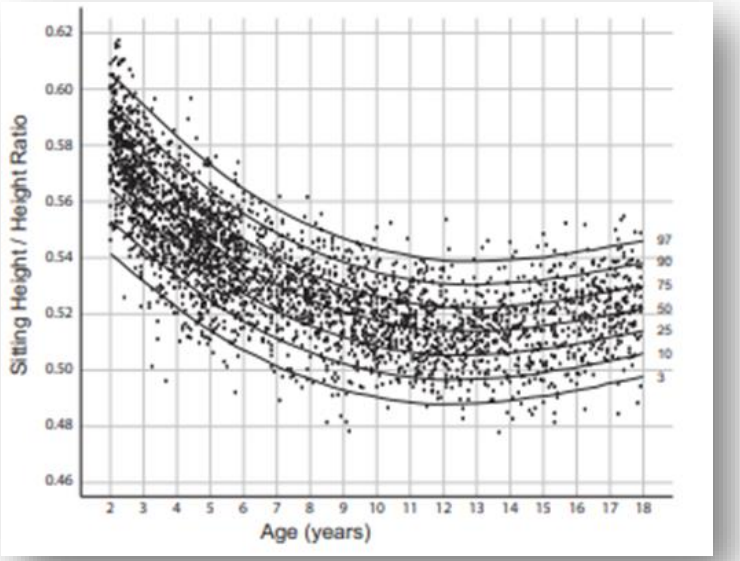
# Consideraciones clínicas en la evaluación de sobrevivientes de cáncer infantil

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# Consideraciones clínicas para el seguimiento

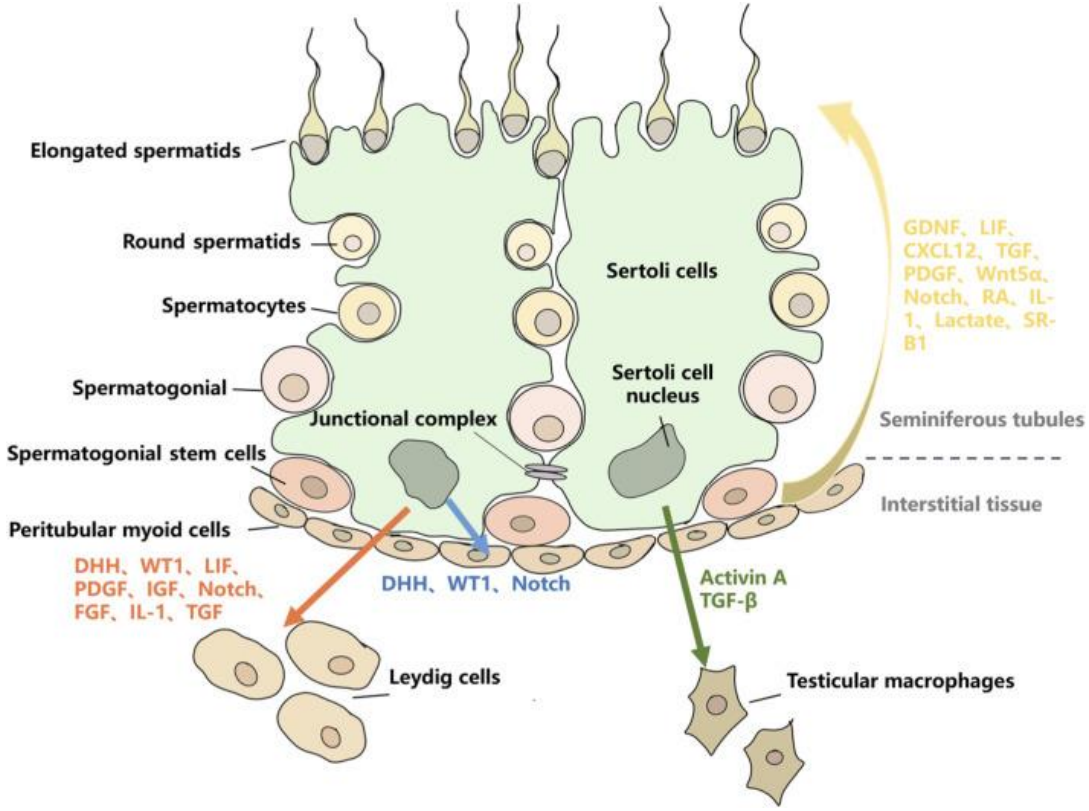
- Crecimiento
  - Crecimiento desproporcionado tras irradiación craneo-espinal o corporal total
  - La talla puede ser engañosamente baja





# Consideraciones clínicas para el seguimiento

- La gonadarquia es el primer signo de pubertad en niños
- Las células Sertoli componen el 70–80 % del volumen testicular
  - son más vulnerables a la radioterapia y a los alquilantes que las células de Leydig
- La hCG estimula el receptor de LH, no el de FSH
  - En tumores de células germinales hay discrepancia

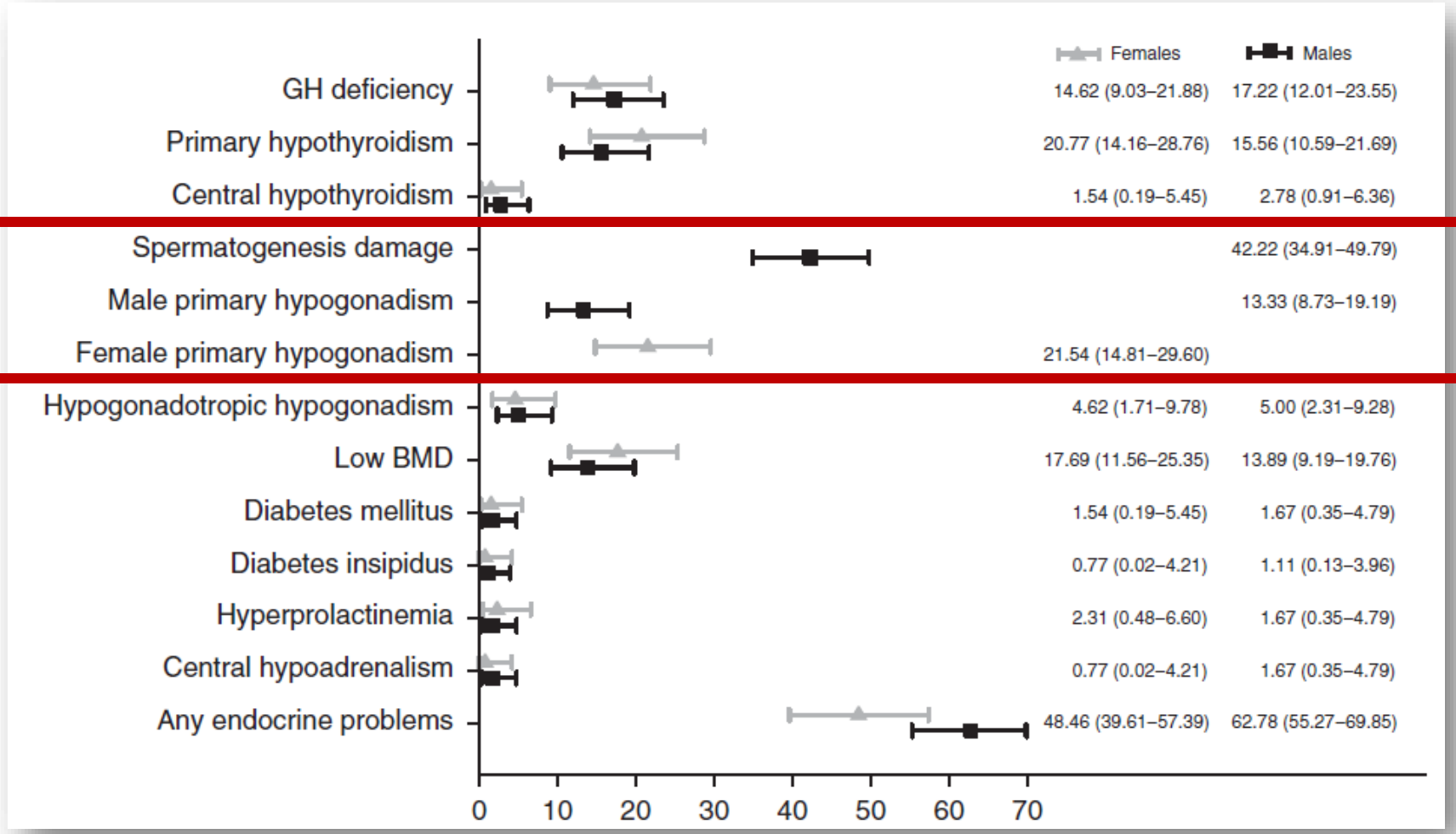



Feng, X. Front Cell Dev Biol. 2025 Dec 10;13:1693878

# La vida después del cáncer: oncofertilidad

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# El hipogonadismo es el trastorno más frecuente en los SCP




Brignardello et al. European Journal of endocrinology. 2013;168:465-72

# Salud reproductiva y preservación de la fertilidad

- Determinante principal de la calidad de vida en los SCP

- Más allá de la fertilidad
  - Baja densidad mineral ósea y crecimiento deficiente
  - Ansiedad y depresión
  - Riesgo de deterioro neurológico
    - Deterioro cognitivo, demencia y parkinsonismo
  - Problemas cardiovasculares

- Ofrecer asesoramiento y preservación de la fertilidad a todos los pacientes

- Uso marginal
  - Carga económica
  - Carácter invasivo de los procedimientos
  - Prioridad del presente inmediato

# Diferencias psicosociales en oncofertilidad



- Mayor malestar emocional por la infertilidad, de mayor duración
- Procedimientos de preservación de la fertilidad más complejos e invasivos
- Mayor necesidad de comunicación y asesoramiento sobre fertilidad



- Malestar por la alteración de la espermatogénesis y la disfunción sexual, menor que en las mujeres
- Retraso del desarrollo psicosocial y preocupaciones sobre las relaciones de pareja
- Mayor satisfacción con la preservación de la fertilidad y el asesoramiento



Psycho-Oncology. 2019;28(3):607-614
Frontiers in Oncology. 2025;15:1515952.

# Estratificación del riesgo en SCP



| | | | Minimally Increased Risk | Significantly Increased risk | High level of Increased risk |
|---|---|---|---|---|---|
| Alkylators CED* gm/m2 | | Prepubertal | CED < 8 | 8-12 | > 12 |
| | | Pubertal | CED < 4 | 4-8 | >8 |
| Heavy Metal | | | Cisplatin Carboplatin | | |
| Hematopoietic Stem Cell Transplant | | | | | Alkylator +/-Total body irradiation Myeloablative and Reduced intensity regimens |
| Radiation exposure | Ovary | Prepubertal | | < 15 Gy | ≥ 15 Gy |
| | | Pubertal | | < 10 Gy | ≥ 10 Gy |
| | Hypothalamus | | 22-29.9 | > 30-39.9 Gy | > 40 Gy |



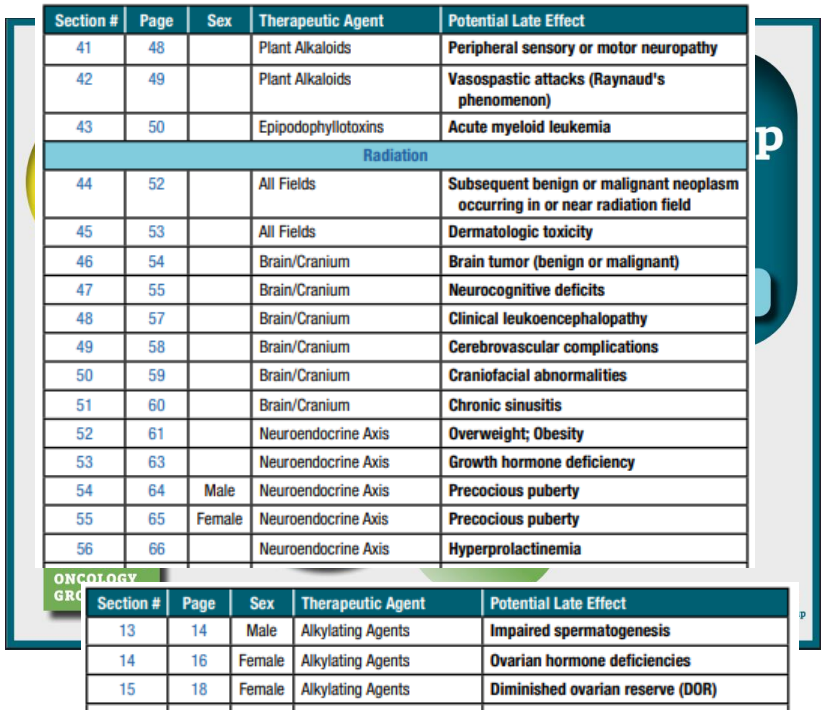
| | | Minimally Increased Risk | Significantly Increased risk | High level of Increased risk |
|---|---|---|---|---|
| Alkylators CED* gm/m2 | | CED < 4 | | CED ≥ 4 |
| Hematopoietic Stem Cell Transplant | | | | Alkylator +/-Total body irradiation Myeloablative and Reduced intensity regimens |
| Heavy Metal mg/m2 | | Cisplatin Carboplatin | Cisplatin > 500 | |
| Radiation Exposure | Testicular | 0.2-0.6Gy | 0.7-3.9 Gy | ≥ 4.0 Gy |
| | Hypothalamus | 26-29.99 | > 30-39.9 Gy | > 40 Gy |
| Surgery | | | RPLND^ | |

JOURNAL OF ADOLESCENT AND YOUNG ADULT ONCOLOGY
Volume 9, Number 6, 2020

# El papel del pediatra general

# El papel del pediatra en los SCP

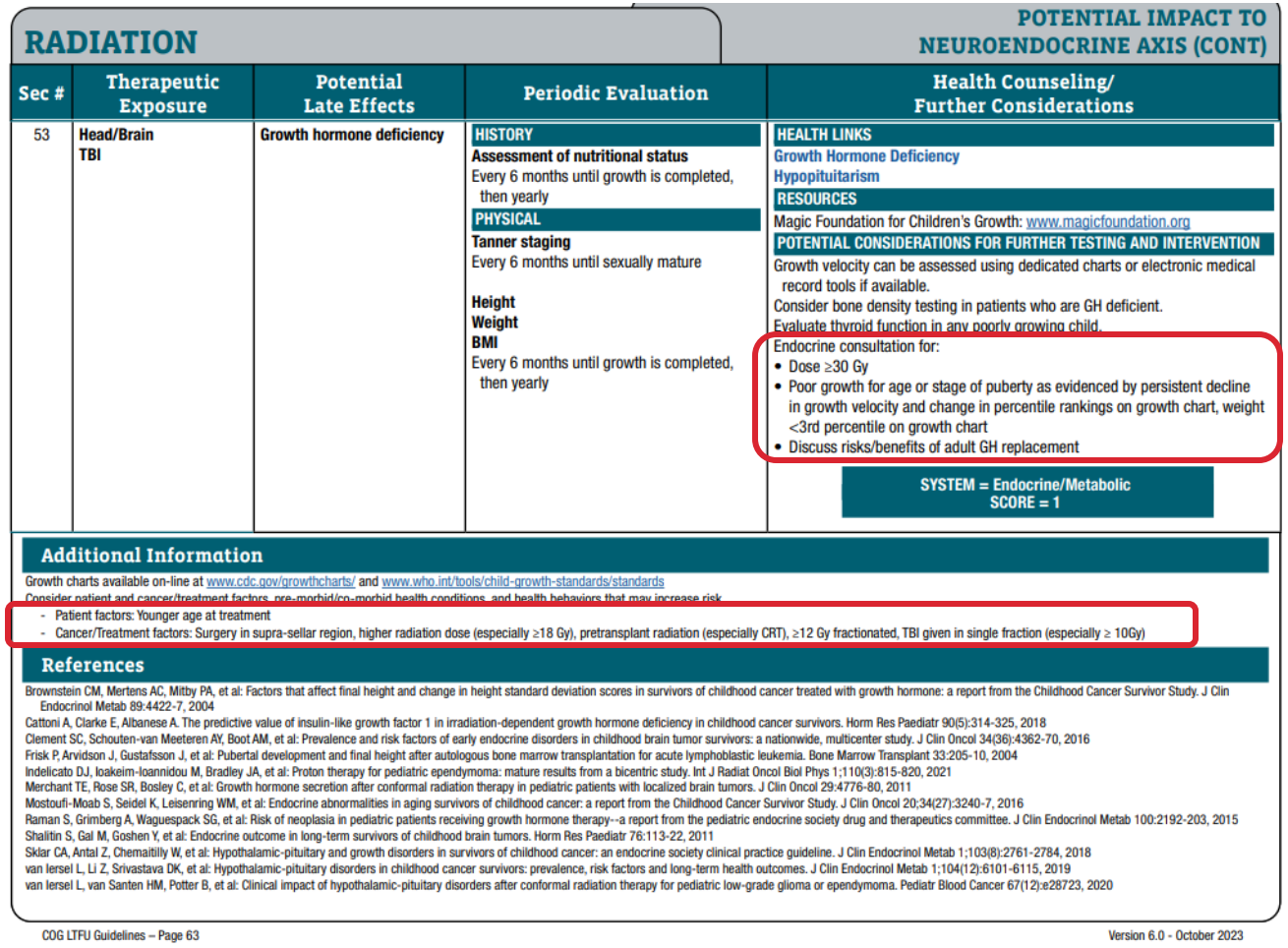
- Guías multidisciplinarias basadas en la evidencia
- Diseñadas para todos los profesionales de la salud



| Section # | Page | Sex | Therapeutic Agent | Potential Late Effect |
|---|---|---|---|---|
| 41 | 48 | | Plant Alkaloids | Peripheral sensory or motor neuropathy |
| 42 | 49 | | Plant Alkaloids | Vasospastic attacks (Raynaud's phenomenon) |
| 43 | 50 | | Epipodophyllotoxins | Acute myeloid leukemia |
| | | | Radiation | |
| 44 | 52 | | All Fields | Subsequent benign or malignant neoplasm occurring in or near radiation field |
| 45 | 53 | | All Fields | Dermatologic toxicity |
| 46 | 54 | | Brain/Cranium | Brain tumor (benign or malignant) |
| 47 | 55 | | Brain/Cranium | Neurocognitive deficits |
| 48 | 57 | | Brain/Cranium | Clinical leukoencephalopathy |
| 49 | 58 | | Brain/Cranium | Cerebrovascular complications |
| 50 | 59 | | Brain/Cranium | Craniofacial abnormalities |
| 51 | 60 | | Brain/Cranium | Chronic sinusitis |
| 52 | 61 | | Neuroendocrine Axis | Overweight; Obesity |
| 53 | 63 | | Neuroendocrine Axis | Growth hormone deficiency |
| 54 | 64 | Male | Neuroendocrine Axis | Precocious puberty |
| 55 | 65 | Female | Neuroendocrine Axis | Precocious puberty |
| 56 | 66 | | Neuroendocrine Axis | Hyperprolactinemia |

| Section # | Page | Sex | Therapeutic Agent | Potential Late Effect |
|---|---|---|---|---|
| 13 | 14 | Male | Alkylating Agents | Impaired spermatogenesis |
| 14 | 16 | Female | Alkylating Agents | Ovarian hormone deficiencies |
| 15 | 18 | Female | Alkylating Agents | Diminished ovarian reserve (DOR) |

# Guías COG de seguimiento a largo plazo



## RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (CONT)

| Sec # | Therapeutic Exposure | Potential Late Effects | Periodic Evaluation | Health Counseling/ Further Considerations |
|---|---|---|---|---|
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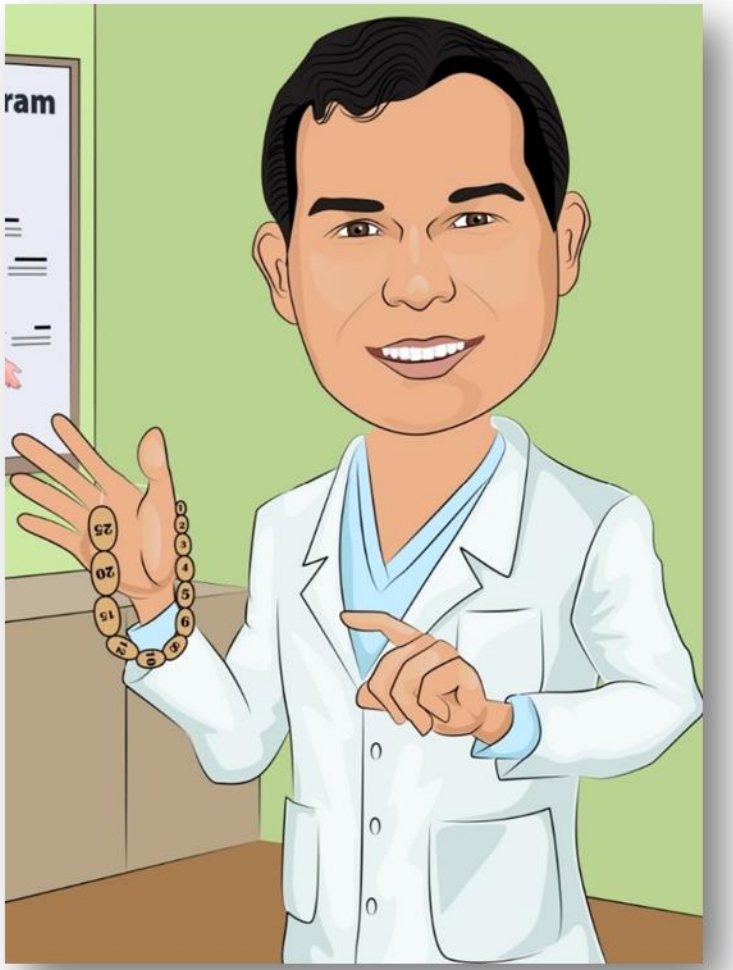
# Conclusiones

1. Las endocrinopatías son prevalentes y variadas en los SCP.

2. Pueden aparecer décadas después del tratamiento y requieren monitoreo a largo plazo.

3. El aumento del número de SCP incrementa la carga de endocrinopatías relacionadas con el cáncer.

4. La endocrinología pediátrica es esencial en el manejo integral. Todos los pediatras deben conocer los efectos endocrinos del cáncer y su tratamiento.



# Preguntas

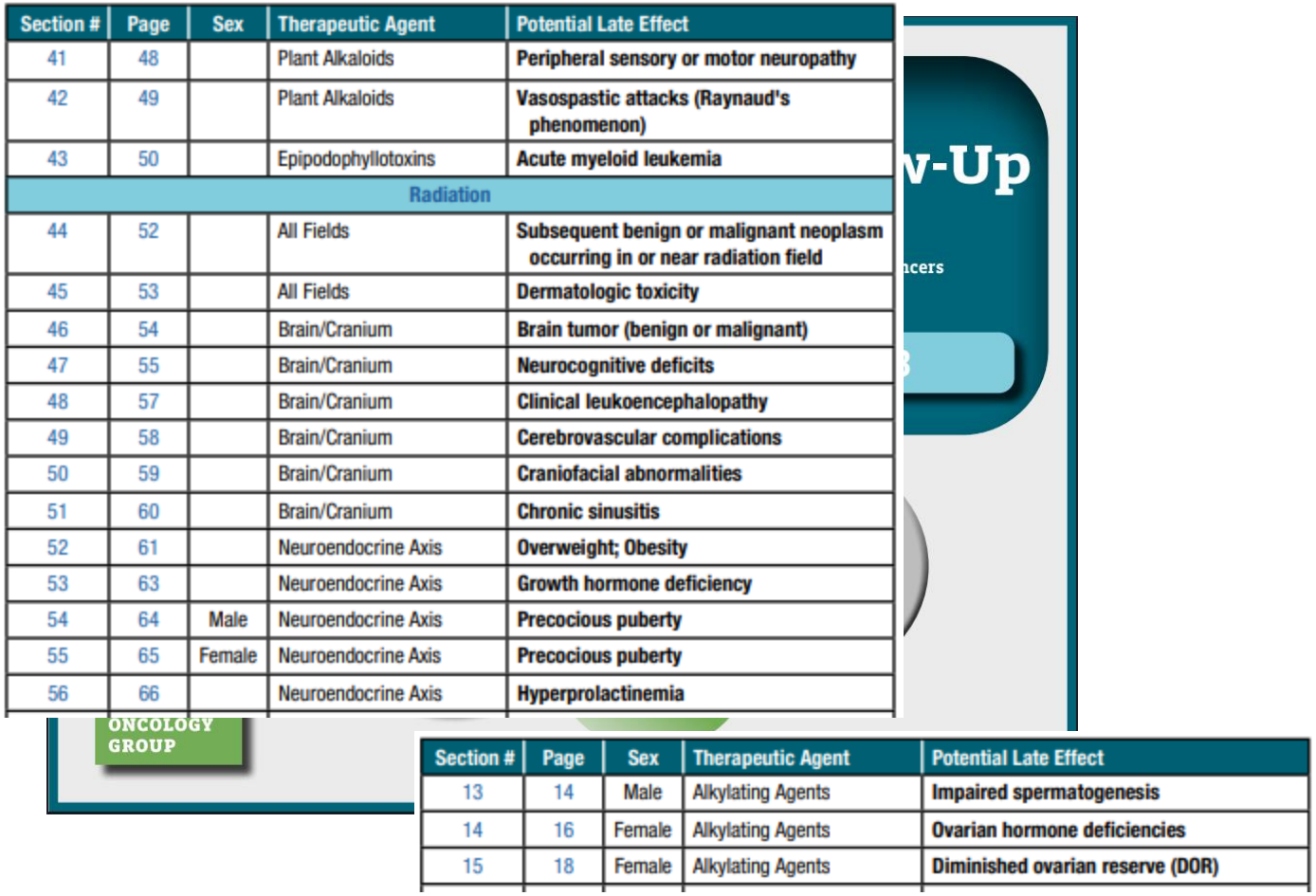
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Baylor College of Medicine
DEPARTMENT OF
PEDIATRICS

# El papel del pediatra

- Guías multidisciplinarias
- Diseñadas para todos los profesionales de la salud



| Section # | Page | Sex | Therapeutic Agent | Potential Late Effect |
|---|---|---|---|---|
| 41 | 48 | | Plant Alkaloids | Peripheral sensory or motor neuropathy |
| 42 | 49 | | Plant Alkaloids | Vasospastic attacks (Raynaud's phenomenon) |
| 43 | 50 | | Epipodophyllotoxins | Acute myeloid leukemia |
| | | | Radiation | |
| 44 | 52 | | All Fields | Subsequent benign or malignant neoplasm occurring in or near radiation field |
| 45 | 53 | | All Fields | Dermatologic toxicity |
| 46 | 54 | | Brain/Cranium | Brain tumor (benign or malignant) |
| 47 | 55 | | Brain/Cranium | Neurocognitive deficits |
| 48 | 57 | | Brain/Cranium | Clinical leukoencephalopathy |
| 49 | 58 | | Brain/Cranium | Cerebrovascular complications |
| 50 | 59 | | Brain/Cranium | Craniofacial abnormalities |
| 51 | 60 | | Brain/Cranium | Chronic sinusitis |
| 52 | 61 | | Neuroendocrine Axis | Overweight; Obesity |
| 53 | 63 | | Neuroendocrine Axis | Growth hormone deficiency |
| 54 | 64 | Male | Neuroendocrine Axis | Precocious puberty |
| 55 | 65 | Female | Neuroendocrine Axis | Precocious puberty |
| 56 | 66 | | Neuroendocrine Axis | Hyperprolactinemia |

| Section # | Page | Sex | Therapeutic Agent | Potential Late Effect |
|---|---|---|---|---|
| 13 | 14 | Male | Alkylating Agents | Impaired spermatogenesis |
| 14 | 16 | Female | Alkylating Agents | Ovarian hormone deficiencies |
| 15 | 18 | Female | Alkylating Agents | Diminished ovarian reserve (DOR) |

[Guías COG de seguimiento a largo plazo]

# Respaldo: página completa de las guías COG

## RADIATION

## POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (CONT)

| Sec # | Therapeutic Exposure | Potential Late Effects | Periodic Evaluation | Health Counseling/ Further Considerations |
|---|---|---|---|---|
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