Endocrine Late Effects in Survivors of Pediatric SCT

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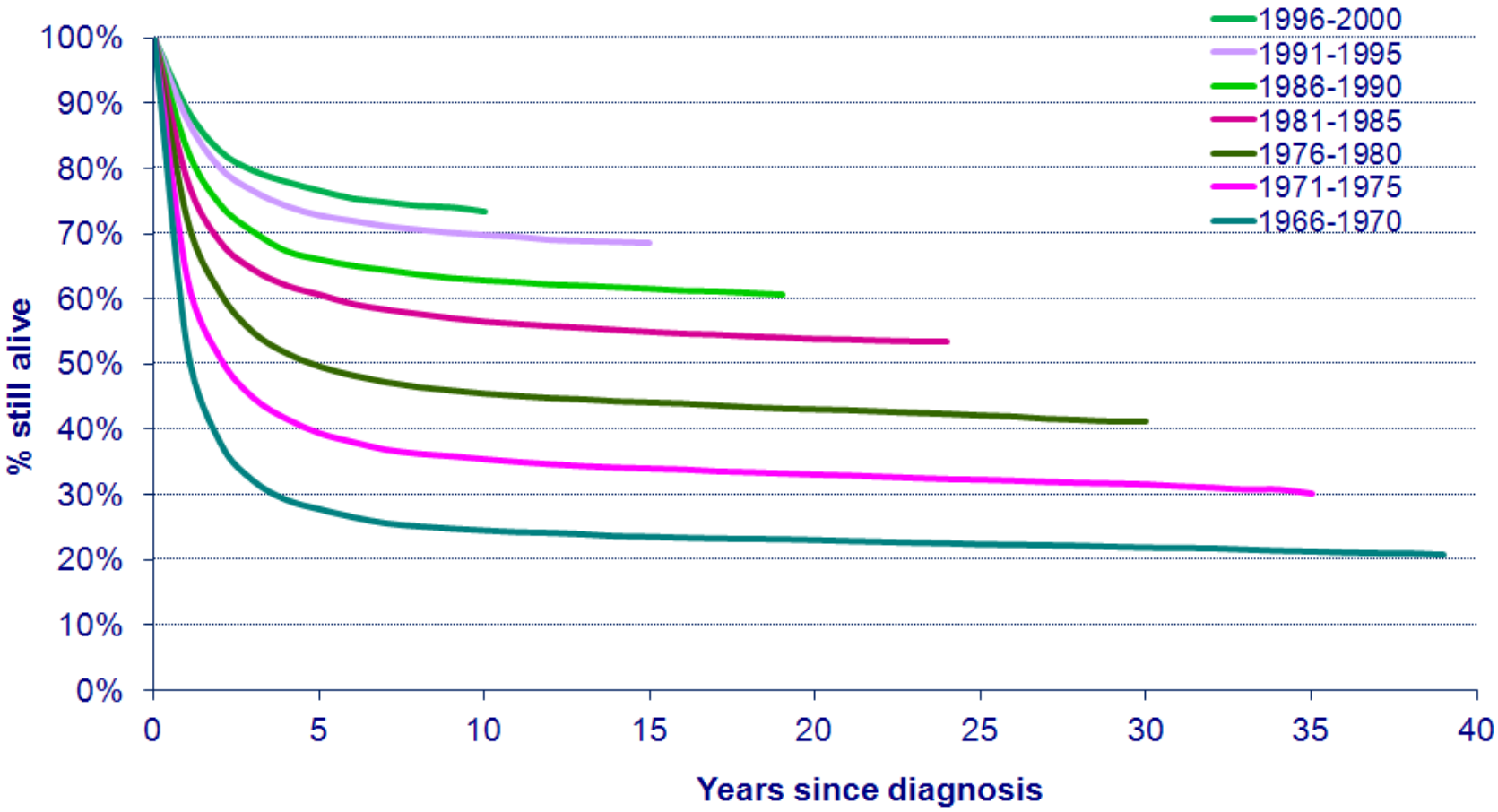
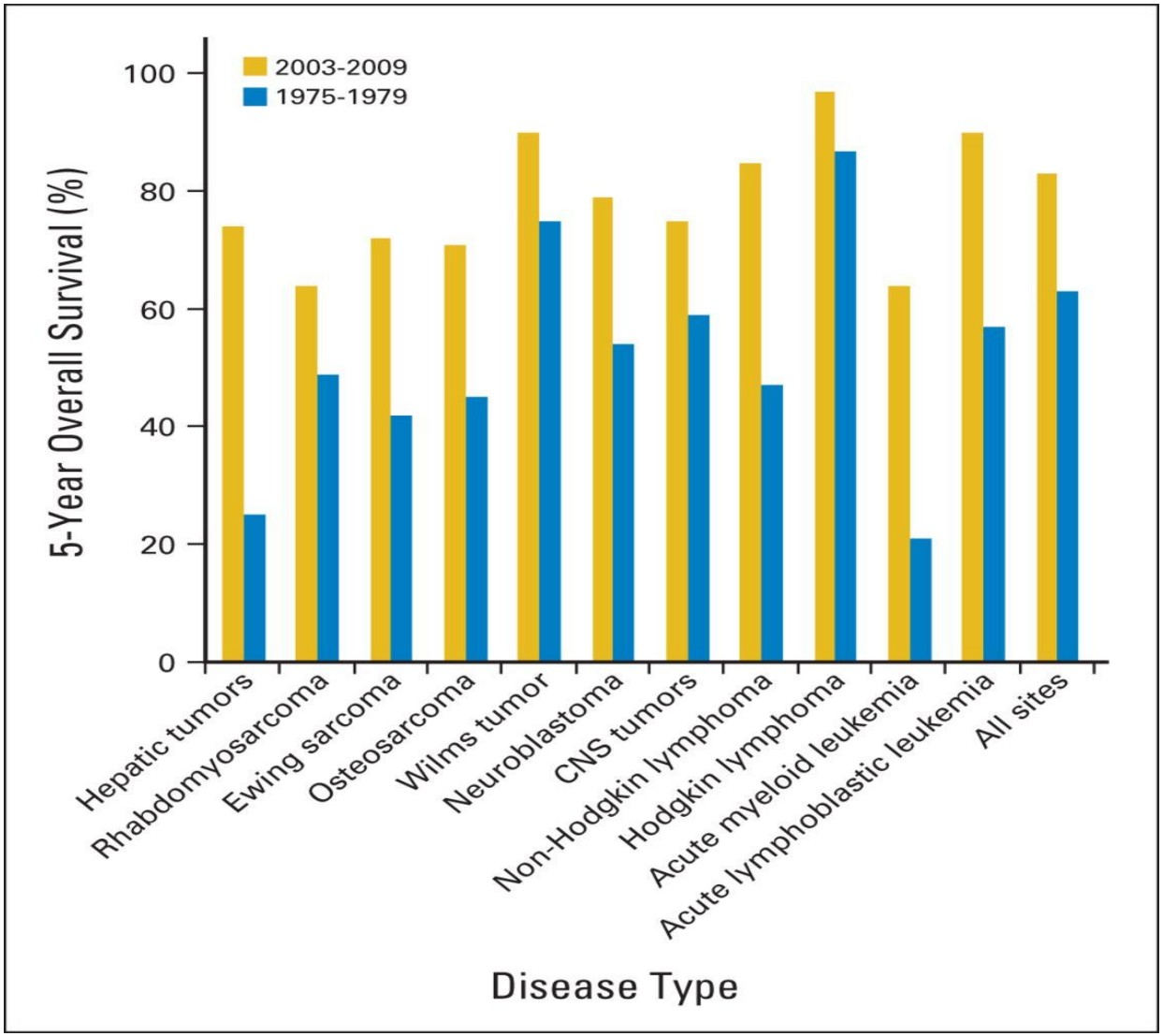
Figure 3.1: Survival of childhood cancer patients diagnosed 1966-2000, by period of diagnosis



Stiller CA (2007). Childhood Cancer In Britain. Oxford University Press, p166, Fig 5.14.

Five-year survival rates for two time periods for pediatric cancer diagnosed from birth to 19 years old.



Hudson M M et al. JCO 2014;32:2391-2397

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Cure Had Not Come Without a Price

- Increasing population of SCT survivors
- Survivors are at risk for chronic or late-occurring health problems caused by their cancer or its treatment
- Thirty years after diagnosis 75% of all survivors will experience at least one late treatment effect

Endocrine Complications

- Most common late effect in survivors of childhood cancer & SCT
- Observed in 20%-50% of survivors
- Followed into adulthood

Risk Factors for Endocrine Dysfunction

- Primary diagnosis & its treatment
- Age at transplant
- Conditioning regimen
- Gender of patient
- Post Transplant exposure; GvHD, Steroids
- Tyrosine kinase inhibitors (TKI)

Endocrine Complications

- Growth impairment
- Thyroid dysfunction
- Puberty
- Gonadal failure
- Metabolic Syndrome

Growth Impairment- Etiology

- Exposure to spinal radiation, TBI
- Chemotherapy treatments
- Age at SCT

- Production of sex hormones
- Hypothyroidism
- Growth hormone (GH) deficiency

- Suboptimal nutrition

Growth Hormone Deficiency

- Hypothalamus/pituitary radiotherapy & TBI
- Radiotherapy- dose and time dependent effect
- Imatinib- tyrosine kinase inhibitor

- Should be investigated when linear growth velocity decelerates over a 6-month period

Evaluation

- Accurate measurement of height
- Measurement of bone age
- Two measurements of GH secretion

- Treatment with rGH replacement therapy is not initiated until 12 months after completing cancer treatment
- Safety of treatment?

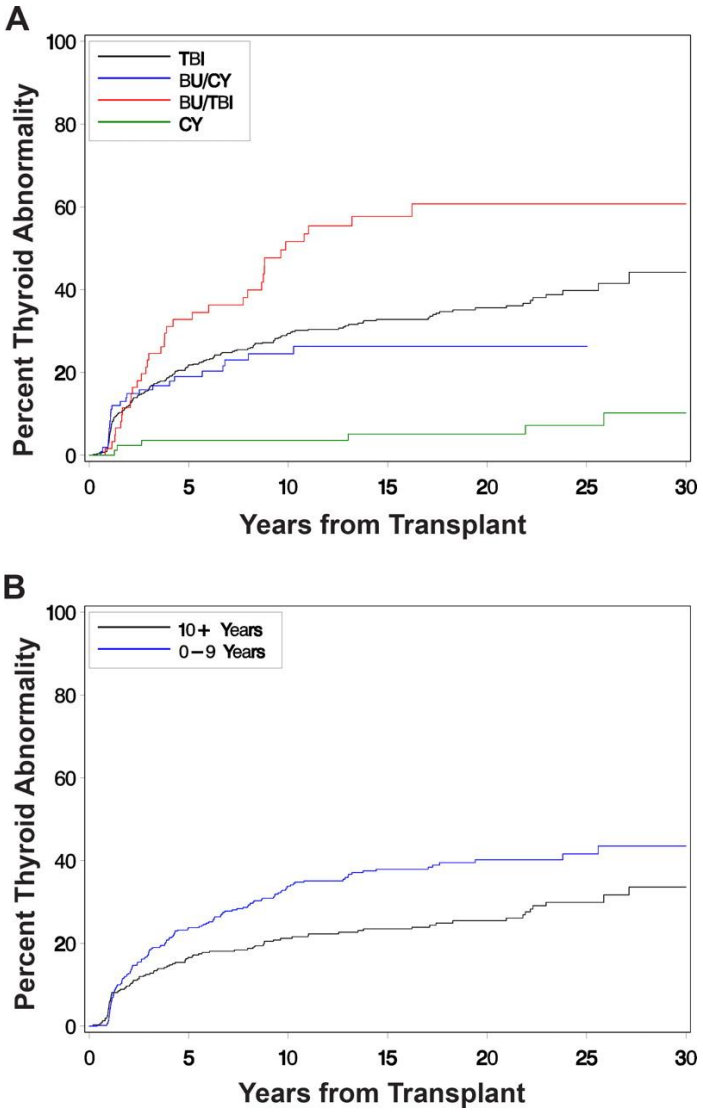
Thyroid Dysfunction

- Hypothyroidism is the most common thyroid abnormality

- Radiation to neck, cranio-spinal & TBI
- Busulfan-based regimens

- TKI- Sorafenib, Sunitinib, Imatinib

Cumulative incidence of developing thyroid dysfunction after HCT in childhood



Sanders J E et al. Blood 2009;113:306-308

blood

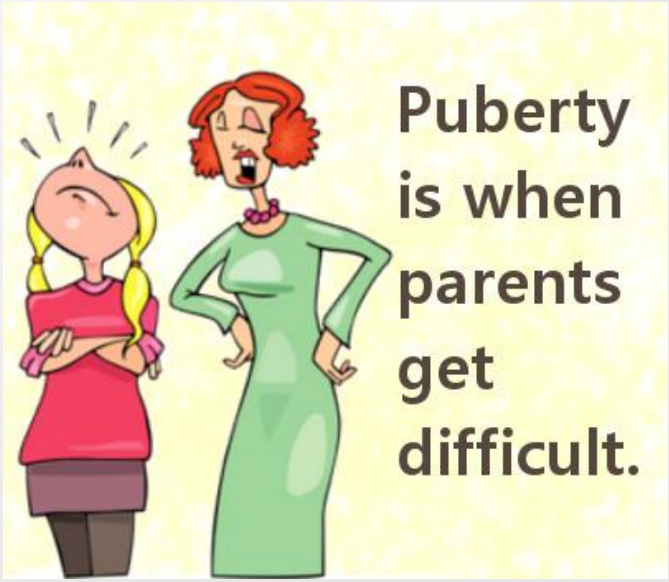
- Surveillance for thyroid dysfunction is crucial
- Hypothyroidism may occur decades later

- TSH, fT4
- Replacement therapy

Puberty

- Substantial changes in gonadal and GH activity
- Development of secondary sexual characteristics
- Increased growth velocity

- Initiation & completion of puberty requires an intact hypothalamic–pituitary–gonadal axis



- Pubertal delay or failure occurs in girls & boys
- Depends on conditioning regimen

- Pubertal development should be carefully monitored after SCT
- Supplemental hormone therapy

Central Precocious Puberty

- Early activation of the hypothalamic–pituitary–gonadal axis
- Onset of puberty prior to the ages of 8-9 years
- Pre-mature closure of growth plates
- Treatment with GnRH agonist

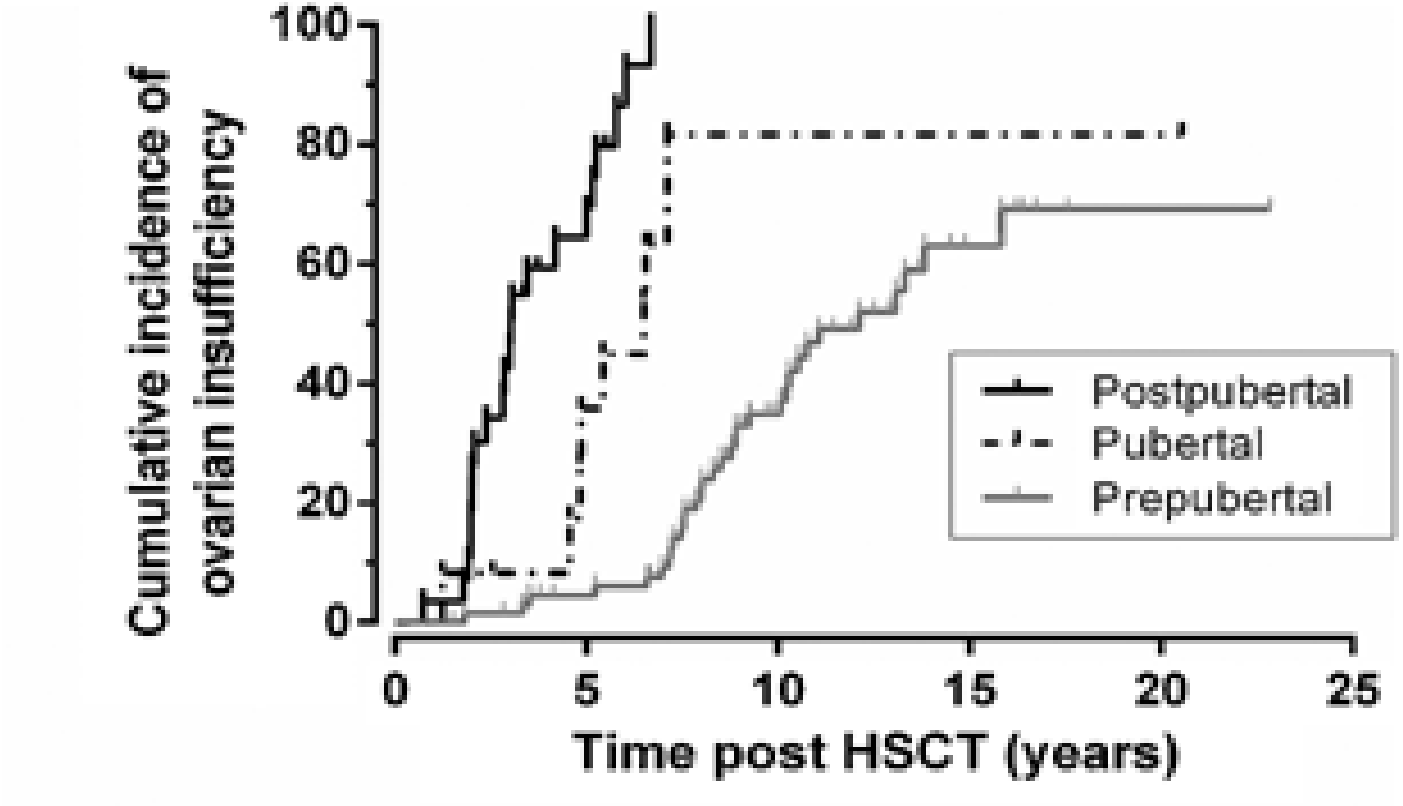
Ovarian Failure

- The ovary is sensitive to the adverse effects of cancer treatments
- Treatments cause a reduction in the ovarian follicle reserve

- Gonadal failure is associated with exposure to CY, BU, and TBI

- Elevated FSH reduced levels of anti-Mu¨llerian hormone (AMH)

Ovarian insufficiency and pubertal development after hematopoietic stem cell transplantation in childhood



Prepubertal	69	61	29	7	1
Pubertal	12	7	1	1	1
Postpubertal	28	6			

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Males

- Germ cells in the testes normally continue to produce sperm during adulthood

- Risk of gonadal failure depends on type of therapy and doses administered

- CY, TBI destroy germ cells within the testes

- Impairment of spermatogenesis may be permanent or temporary
- Recovery is related to agent and dose received
- Many (48%-85%) males who undergo SCT will experience testicular failure with azoospermia

Fertility Preservation in Children & Adolescence

Preserving children's fertility: children's right to an open future

Males

- Sperm banking
- Testicular tissue

cryopreservation so far, this has not led to live births

Females

- Embryo or oocyte cryopreservation
- Ovarian tissue cryopreservation

The only option for pre-pubertal and young females

Pediatric-Specific HCT Long-Term Follow-Up Guidelines

EBMT
European Society for Blood and Marrow Transplantation

ASBMT
American Society for Blood and Marrow Transplantation

PanCareSurFup
Pancare Childhood and Adolescent Cancer Survivor Care and Follow-up Studies

REPORT

NCI, NHLBI/PBMTC First International Conference on Late Effects after Pediatric Hematopoietic Cell Transplantation: Endocrine Challenges—Thyroid Dysfunction, Growth Impairment, Bone Health & Reproductive Risks

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K. Scott Baker,[3] Michael A. Pulsipher,[5] Anna Petryk[6]

The endocrine system is highly susceptible to damage by high-dose chemotherapy and/or irr
hematopoietic cell transplantation (HCT) during childhood. The specific endocrine organs m
HCT include the thyroid gland, the pituitary, and the gonads. In addition, hormones
development and stability of the skeletal system are also affected. Insufficiency of thyroid h
the most common late sequelae of HCT, and occurs more often in young children. De
pituitary's production of growth hormone is a problem of unique concern to the pediat
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COG Guidelines

Nurses Role in Long-Term follow-up

- Multidisciplinary team
- Coordinate care
- Age specific
- Education on disease, late effects, health behavior
- Counseling

Conclusions

- Need for information on disease & side effects
- Importance of life-long follow-up care
- Need for international guidelines

- Transition to adult care

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