

Gynecomastia as a late complication of childhood cancer that can affect the quality of life of male survivors

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 First of all,



Background

- Treatment of cancer in children can be associated with a variety of long-term complications
- Over the past 30 years, the 5year OS for children with cancer has increased from less than 60% to more than 80%.
- As treatment progress and new drug introduced Continuing care of survivors is important
- All RX ... radiation therapy, surgery, or chemotherapy reduce both germ cells and endocrine gonadal function among male survivors of malignancy



Gynecomastia

- Gynecomastia usually presents as subareolar swelling that is compressible, soft, and flexible without nipple retraction or discharge
- Gynecomastia can result from changes in estrogen-androgen balance,
- Potential strategies for reducing late mortality in survivors of childhood cancer include increasing the efficiency and accuracy of screening methods

Endocrine and gonadal dysfunction as the late effects in survivors of malignancy

- Radiation therapy can adversely influence The hypothalamic-pituitary axis? it is very sensitive to radiation.
- Risk factors for hormonal dysfunction include the **total dose of radiation**.
- Growth hormone deficiency is the most common neuroendocrine disturbance.

Gynecomastia

- **Hypothyroidism** is the most common **nonmalignant** late effect of malignancy
- **Spermatogonia** and the germ cells in the ovaries are **sensitive to radiation**, and certain types of chemotherapy, particularly **cyclophosphamide** and other **alkylating agents**
- Gynecomastia as a late complication of male cancer survivors often presents **psychologic challenges**

Etiologies of Gynecomastia

The etiologies of gynecomastia with their prevalence in male adolescence

Causes of gynecomastia	Frequency
Pubertal gynecomastia	25%
Idiopathic gynecomastia	25%
Drug-Induced gynecomastia	10-25%
Cirrhosis or malnutrition	8%
Primary hypogonadism	8%
Testicular tumors	3%
Secondary hypogonadism	2%
Hyperthyroidism	2%
Chronic kidney disease	1%
Others	6%

Case of Gynecomastia



- A **13-year old boy** who was a known case of right forearm alveolar rhabdomyosarcoma stage 3 and group 1 according to COG
- He received a full course of **chemotherapy**(VAC) as an intermediate risk group in addition to radiotherapy after complete local resection with free margin with no evidence of metastasis.
- **After 6 months** of cessation of chemotherapy, he referred due to unpleasant feelings of bilateral breast enlargement without pain or discharge that **affect social relationships and consequently quality of life.**

Chemotherapeutic agents that cause gynecomastia

- Alkylating Agents,
- Nitrosoureas,
- Vincristine,
- Imatinib,
- Methotrexate,
- Cisplatin.

Other drugs

- Cimetidine,
- Ranitidine,
- Proton Pump Inhibitors

Patients being treated with chemotherapy may **simultaneously receive non-chemotherapy agents** that can cause gynecomastia, including cimetidine, ranitidine, and omeprazole, these agents also may **worsen the gynecomastia** induced by chemotherapeutic agents

The pathogenesis of gynecomastia

- The pathogenesis of gynecomastia appears to principally arise from an **imbalance of the androgenic and estrogenic** effects on breast tissue.
- Estrogens increase the proliferation of breast tissue, while androgens inhibit proliferation. **Both types of hormone receptors** exist in the normal male breast tissue.
- Therefore, gynecomastia occurs with deficiency of androgens, or an increase in levels of estrogen
- **The most common findings include** increased LH and FSH with normal or low-normal level of testosterone.

The clinical approach to gynecomastia as a late complication in childhood cancer survivors

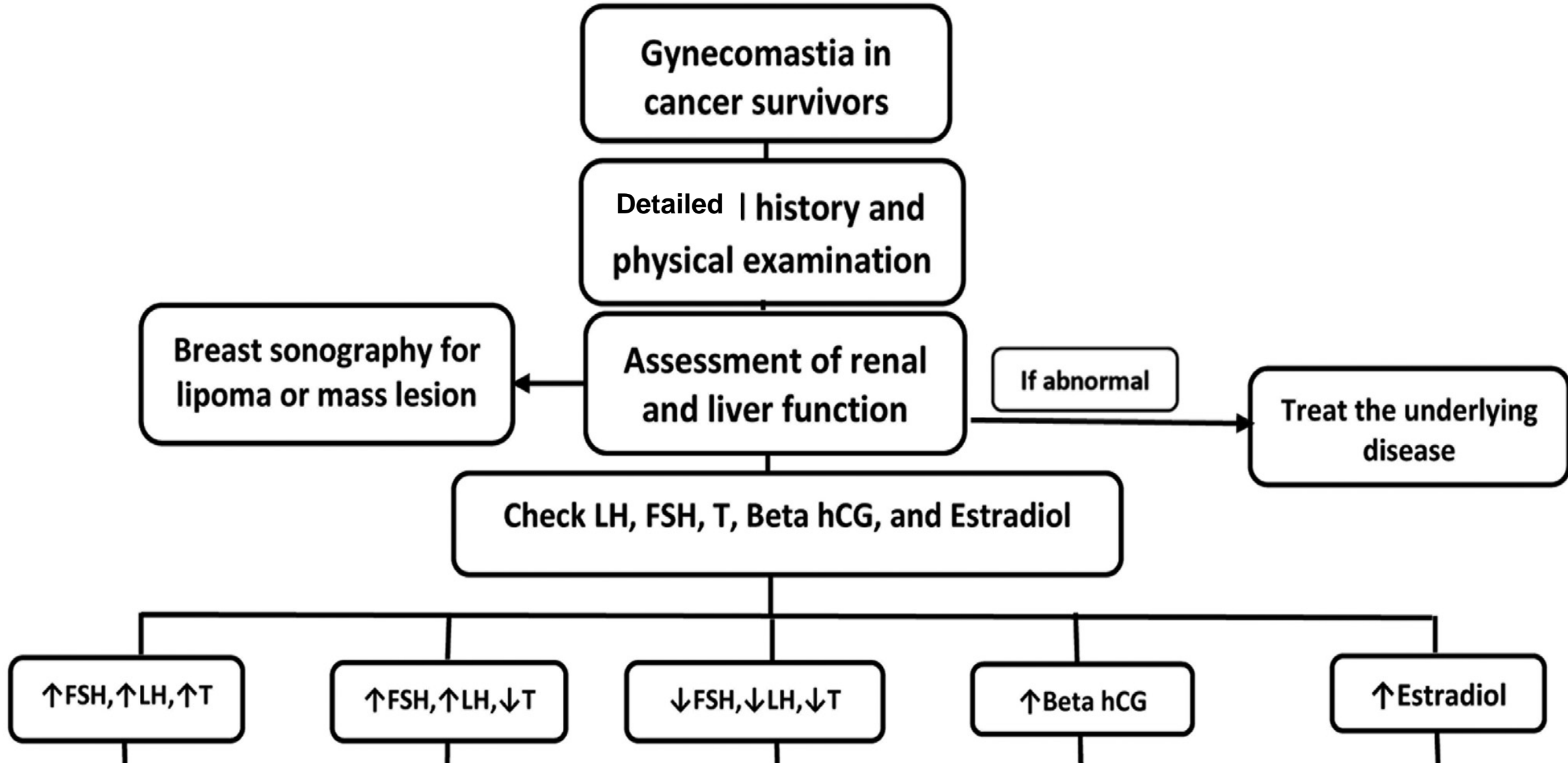
• History and Detailed Physical Examination

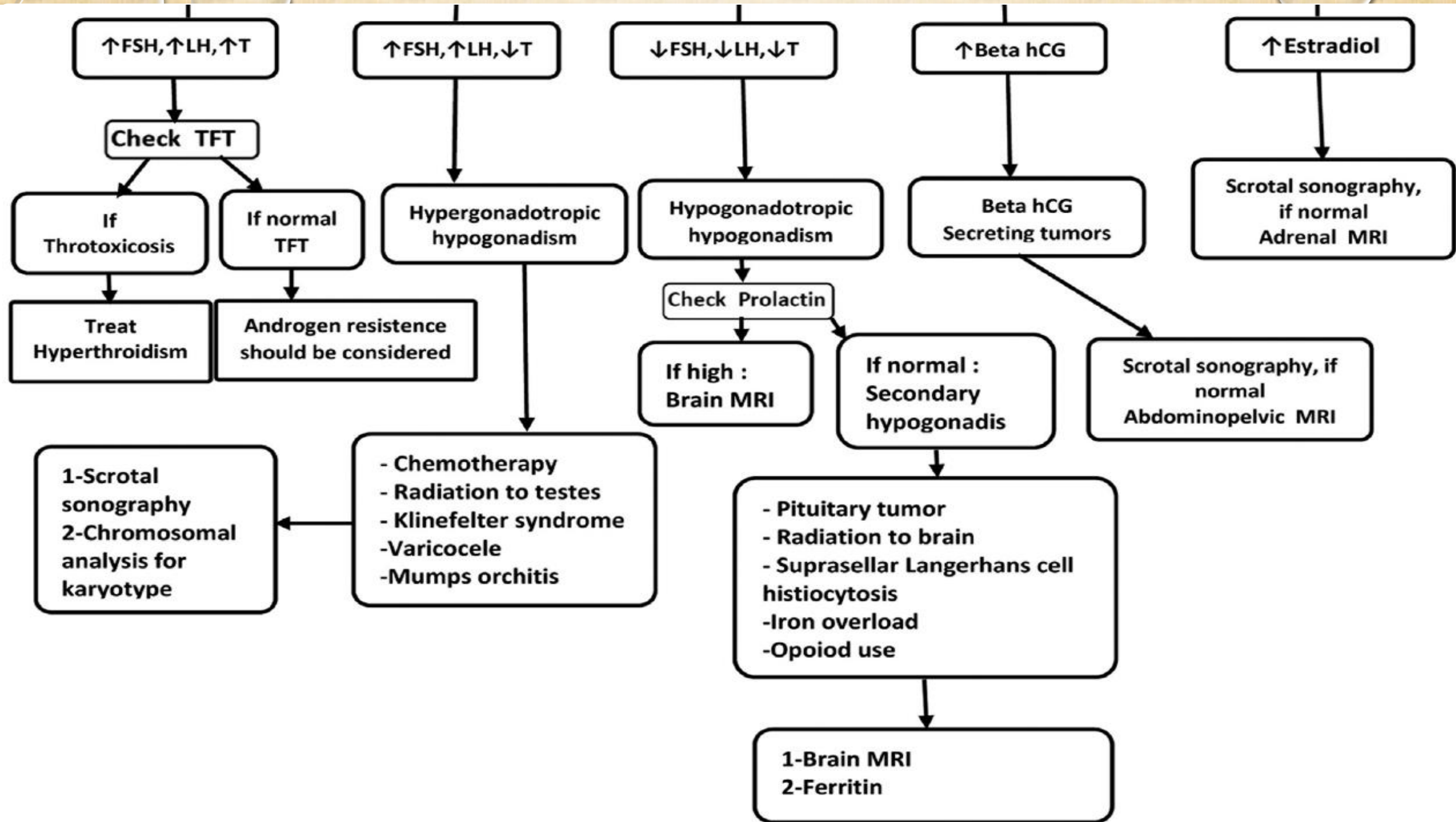
- In the history,
- The duration of gynecomastia
- The family history
- The existence of associated symptom, for example, pain or discharge from the nipple;
- The type and cumulative dose of chemotherapeutic agent, especially cyclophosphamide
- The location and dose of radiotherapy
- The coexistence of a chronic illness such as liver disease, renal disease, and hyperthyroidism
- Current medications with attention to those that may cause or help promote gynecomastia in someone who might have a predisposing factor
- How this problem is affecting psychosocial well-being

The health care provider must pay special attention to:

- (1) a detailed breast examination;
- (2) tanner stage; and
- (3) the size of the testes

Guideline based approach





The treatment of gynecomastia in cancer survivors

- The treatment of drug-induced gynecomastia includes **both medical and surgical** approaches
- The duration of gynecomastia, a breast size of more than 10 cm, tanner stage ≥ 3 , and psychosocial impairment of patients are the main factors for determining the type of treatment

Medical treatments include antiestrogen (tamoxifen, raloxifene, and clomiphene), testosterone therapy, and danazol.

If the duration of gynecomastia is more than 1 year because of fibrous tissue formation, then medical treatments have no benefits

Surgical mastectomy is recommended in cases that have had gynecomastia for more than 1 year, especially if there is no improvement after medical therapy

➤ We would like to express my deepest appreciation to....
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THANK YOU !