**SUBACUTE THYROIDITIS**

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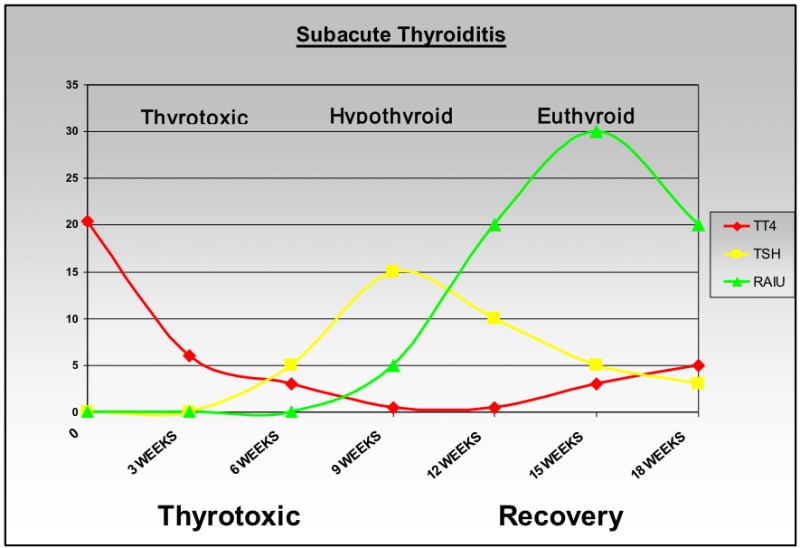
**CLINICAL RECOGNITION**

Subacute thyroiditis (SAT) is an inflammatory condition of the thyroid with characteristic presentations and clinical course. Patients with the classic, painful (DeQuervain’s; Granulomatous) thyroiditis, (PFSAT) typically present with painful swelling of the thyroid. Transient vocal cord paresis may occur. At times, the pain begins and may be confined to the one lobe, but usually spreads rapidly to involve the rest of the gland ("creeping thyroiditis"). Pain may radiate to the jaw or the ears. Malaise, fatigue, myalgia and arthralgia are common. A mild to moderate fever is expected, and at times a high fever of 104°F (40.0°C) may occur. The disease process may reach its peak within 3 to 4 days and subside and disappear within a week, but more typically, onset extends over 1 to 2 weeks and continues with fluctuating intensity for 3 to 6 weeks. The thyroid gland is typically enlarged, smooth, firm and tender to palpation, sometimes exquisitely so. Approximately one-half of the patients present during the first weeks of the illness, with symptoms of thyrotoxicosis. Subsequently patients often experience hypothyroidism before returning to normal (see [figure 1](https://www.ncbi.nlm.nih.gov/books/NBK279084/figure/emergencies_subacute-thyroiditis.F1/?report=objectonly)). This painful condition lasts for a week to a few months, usually demonstrates a very high erythrocyte sedimentation rate (ESR), elevated C- reactive protein (CRP) levels, and has a tendency to recur.

Painless (silent, autoimmune) subacute thyroiditis (PLSAT) occurs spontaneously or following pregnancy when it is referred to as postpartum thyroiditis [PPT]). Autoimmune thyroiditis is histologically similar to Hashimoto's thyroiditis and occurs following 3.9-10% of pregnancies. The combination of thyroid enlargement usually without discomfort and positive anti-thyroid antibodies, associated with typical thyroid function test abnormalities (see [figure 1](https://www.ncbi.nlm.nih.gov/books/NBK279084/figure/emergencies_subacute-thyroiditis.F1/?report=objectonly)), over a 9-12 month course should alert the clinician to the presence of PLSAT.

**PATHOPHYSIOLOGY**

A tendency for the painful form of the disease to follow upper respiratory tract infections or sore throats has suggested a viral infection. An autoimmune reaction is possible as patients with PFSAT often manifest HLA-Bw35 and those with PLSAT are frequently TPO or TG-ab positive. In both forms, clinical thyroid symptoms result from either the initial release of thyroid hormone from the inflamed tissue during the thyrotoxic phase or the lack of circulating thyroid hormones in the hypothyroid phase (See [figure 1](https://www.ncbi.nlm.nih.gov/books/NBK279084/figure/emergencies_subacute-thyroiditis.F1/?report=objectonly)). Medications associated with SAT are summarized in [table 4](https://www.ncbi.nlm.nih.gov/books/NBK279084/table/emergencies_subacute-thyroiditis.T.cause/?report=objectonly).



**Figure 1. Time Course of Subacute Thyroiditis**

**DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS**

Subacute thyroiditis is a diagnosis made clinically. Anterior neck pain, preceded by an upper respiratory inflammation, alerts the clinician to the classic PFSAT. Differential diagnostic considerations include acute (suppurative, thyroid abscess) thyroiditis (see [table 1](https://www.ncbi.nlm.nih.gov/books/NBK279084/table/emergencies_subacute-thyroiditis.T.featu/?report=objectonly)), which is usually a painful nodular enlargement of the thyroid or unusual presentations of Graves’ or nodular thyroid disease (see [table 2](https://www.ncbi.nlm.nih.gov/books/NBK279084/table/emergencies_subacute-thyroiditis.T.diffe/?report=objectonly) below) with pain generated by capsular stretching.

Thyroid function tests (see [table 3](https://www.ncbi.nlm.nih.gov/books/NBK279084/table/emergencies_subacute-thyroiditis.T.diffe_1/?report=objectonly)) during the painful (initial) phase of SAT often reveal a suppressed TSH and elevation of total T4 and T3 levels consistent with the thyrotoxic state. T3 (ng/dl) to T4 (ug/dl) ratio is less than 20 in all forms of SAT. ESR is almost always greater than 50 and WBC counts and CRP levels are usually elevated in PFSAT. PLSAT (including PPT) is typically associated with the presence of anti-thyroid peroxidase (TPO-ab) and thyroglobulin (Tg-ab) antibodies, both of which are usually absent or present only in low titers in PFSAT. Thyrotropin receptor antibodies (TRAb) are usually positive in Graves' disease and absent or low level in patients with PFSAT as well as PPT.

Radioactive iodine uptake and scan typically reveals a low RAIU and poor visualization of the thyroid in PFSAT and PLSAT whereas significant uptake is expected in Graves’ disease (GD) or toxic nodular goiters (TNG). PLSAT must be differentiated from other forms of low uptake thyrotoxicosis (see [Table 2](https://www.ncbi.nlm.nih.gov/books/NBK279084/table/emergencies_subacute-thyroiditis.T.diffe/?report=objectonly)). Iatrogenic thyrotoxicosis (factitious [l-thyroxine (LT4), l-triiodothyronine (LT3) or T4/T3 combination] results in a suppressed thyroglobulin (TG) level. Ectopic thyroid hormone production in a Struma Ovarii or functional metastatic thyroid cancer can be detected with total body scanning. Iodine contamination after a contrast enhanced CT, obliterates the RAIU and obscures the presence of the more frequently encountered Graves’ disease or a toxic multinodular goiter. A recent CT scan will frequently alert the clinician to this artifact. Urine iodine measurement can quantify the degree of iodine contamination present.

Thyroid ultrasound typically shows a heterogeneously hypoechoic pattern and has a suppressed vascular pattern in SAT while patients with Graves’ disease demonstrate hyper-vascularity. The presence of thyroid nodules supports the presence of a toxic nodular goiter. Localized PFSAT, can be suggestive of thyroid cancer. Usually the pain, elevated erythrocyte sedimentation rate and leukocytosis, and clinical remission or spread to other parts of the gland make clinical differentiation possible but may require a fine needle aspiration for definitive diagnosis.

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| **Table 1. Features Useful in Differentiating Acute Suppurative Thyroiditis (AST) and Subacute Thyroiditis (SAT)** | | |
| **Characteristic** | **AST** | **SAT** |
| Prior URI | 88% | 17% |
| Fever | 100% | 54% |
| Symptoms of Hyperthyroidism | Uncommon | 47% |
| Sore throat | 90% | 36% |
| Painful thyroid swelling | 100% | 77% |
| Left side affected | 85% | not specific |
| Migrating tenderness | Possible | 27% |
| Erythema of skin | 83% | not usually |
| Elevated WBC count | 57% | 25-50% |
| Elevated ESR | 100% | 85% |
| Abnormal TFTs | 5-10% | 60% |
| Enzymes- Alk-phos.**↑**, AST/ALT **↑** | Rare | common |
| FNA Purulent, bacteria or fungi present | ~100% | 0 |
| Lymphocytes, macrophages, PNMs, giant cells | 0 | ~100% |
| 123I uptake low | Rarely | ~100% |
| Abnormal thyroid scan | 92% | — |
| Scan / US helpful in D/D | 75% | Non-specific |
| Gallium scan positive | ~100% | ~100% |
| Barium swallow = fistula | Common | 0 |
| CT scan useful | Rarely | not useful |
| Clinical response to glucocorticoid treatment | Transient | 100% |
| Incision/drainage required | 85% | No |
| Recurrence following operative drainage | 16% | No |
| Pyriform sinus fistula discovered | 96% | No |

URI= Upper Respiratory Infection, WBC= white blood cell count, ESR= Erythrocyte Sedimentation Rate, TFT’s= Thyroid function tests, Alk-Phos= Alkaline Phosphatase, AST= Aspartate Aminotransferase, ALT= Alanine Aminotransferase, FNA= Fine needle aspiration, US= Ultrasound examination, ↑= elevated

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| **Table 2. Differential Diagnosis of Thyrotoxic Patients Based on Radioactive Iodine Uptake (RAIU)** | |
| **Normal to ↑ 123-I RAIU** | **Near absent 123-I RAIU** |
| Graves’ disease | Painless (silent) thyroiditis |
| Toxic multinodular goiter | Amiodarone-induced thyroiditis |
| Toxic solitary nodule | Subacute (painful) thyroiditis |
| Trophoblastic (hCG mediated) disease | Iatrogenic or factitious thyrotoxicosis |
| TSH-producing pituitary tumor | Ectopic tissue (Struma Ovarii, functional cancer) |
| Thyroid hormone resistance | Acute thyroiditis |

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| **Table 3. Differential Diagnostic Considerations in the Thyrotoxic Patient (Typical findings in each disease)** | | | | |
|  | **PFSAT** | **PLSAT** | **PPT** | **Graves’** |
| Neck Pain | Yes | No | No | No |
| Recent URI | Yes | No | No | No |
| Systemic symptoms | Yes | No | No | No |
| Recent Pregnancy | No | No | Yes | No |
| Thyroid symptoms | Yes | Yes | Yes | Yes |
| ESR | Elevated | Normal | Normal | Normal |
| CRP | Elevated | Normal | Normal | Normal |
| TSH | ↑/ ↓/ Nl | ↑/ ↓/ Nl | ↑/ ↓/ Nl | Suppressed |
| FT4 | ↑/ ↓/ Nl | ↑/ ↓/ Nl | ↑/ ↓/ Nl | Nl/↑ |
| TT3 | ↑/ ↓/ Nl | ↑/ ↓/ Nl | ↑/ ↓/ Nl | Nl/ ↑ |
| T3/T4 | < 20 | < 20 | < 20 | > 20 |
| Thyroglobulin | Elevated | Elevated | Elevated | Elevated |
| TPO-ab | Negative | +/−, Pos | +/−, Pos | +/−, Pos |
| Tg-ab | Negative | +/−, Pos | +/−, Pos | +/−, Pos |
| TSHR-ab | Negative | Neg | Neg | Pos |
| RAIU/Scan | Low/ Not visible | Low/ Not visible | Low/ Not visible | High/ diffuse |
| US Echogenicity | Hypo- echoic | Hypo- echoic | Hypo- echoic | Hypo- echoic |
| Vascularity | Decreased | Decreased | Decreased | Increased |

PFSAT= painful subacute thyroiditis; PLSAT= painless subacute thyroiditis; PPT= postpartum thyroiditis

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| **Table 4. Causes of Drug Associated Thyrotoxicosis** | | | |
| **Drug** | **Mechanism** | **Timing** | **Therapy** |
| Amiodarone | Iodine (AIT 1) | months to years | Supportive, ATDs, Perchlorate, Surgery |
| Amiodarone | Thyroiditis (AIT 2) | Often > 1 year | Supportive care, Surgery, Prednisone |
| Lithium | Thyroiditis | Often > 1 year | ATDs, Supportive |
| Interferon-α | Thyroiditis or Graves’ | Months | Supportive, ATDs, and /or 131-I (Graves’ only) |
| Interleukin-2 | Thyroiditis or Graves’ | Months | Supportive, ATDs, and /or 131-I (Graves’ only) |
| Contrast (I) | Thyroid autonomy | Weeks to months | ATDs |
| 131-I Ablation | Destructive thyroiditis | 1-4 weeks | Supportive, prednisone |
| 131-I Rx of TMNG | Graves’ disease | 3-6 months | 131-I, surgery, ATDs |
| Check Point Inhibitors | Thyroiditis or autoimmune | Weeks to months | Supportive, 131-I, surgery, ATDs |
| Tyrosine Kinase Inhibitors | Thyroiditis | Weeks to months | Supportive |

ATD= Anti thyroid drugs, TMNG= Toxic Multinodular Goiter

**THERAPY**

In some patients, no treatment is required. For many, analgesic therapy for relief of pain can be achieved with non-steroidal anti-inflammatory agents. If this fails, prednisone administration should be employed with daily doses of 20-40 mg prednisone. After one to 2 weeks of this treatment, the dosage is tapered over a period of 6 weeks. Most patients have no recrudescence of symptoms, but occasionally this does occur and the dose must be increased again. The recurrence rate of painful subacute thyroiditis after cessation of prednisone therapy is about 20%. Beta blocking agents are usually administered for relief of thyrotoxic symptoms in the initial stage of SAT. Antithyroid drugs have no role in the management of established SAT as the excess thyroid hormone levels result from release of preformed thyroxine and triiodothyronine from inflamed tissue. Levothyroxine administration may be useful, at least transiently, if the patient enters a phase of hypothyroidism. Surgical intervention is not the primary treatment for subacute thyroiditis but is safe and with low morbidity, if necessary, because of the possibility of associated papillary cancer based on cytological examination.

**FOLLOW-UP**

In 90% or more of patients with classic painful subacute thyroiditis, there is a complete and spontaneous recovery and a return to normal thyroid function. However, the thyroid glands of patients with subacute thyroiditis may exhibit irregular scarring between islands of residual

functioning parenchyma. Up to 10% of the patients may become hypothyroid and require permanent replacement with levothyroxine. Rates of permanent hypothyroidism after antibody positive PLSAT and especially PPT are significantly higher.

**GUIDELINES**

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