Lymphadenopathy Workup

Most nodes are reactive, which is exactly why the few that are not get watched too long

Location beats size
and supraclavicular is never "watch it"

⚠ THE NODE YOU NEVER OBSERVE

⚠ SUPRACLAVICULAR

Malignancy risk ~90% over age 40, ~25% under 40 -the highest-risk site by a wide margin. **Investigate ANY supraclavicular node regardless of size, tenderness or duration.** "Small and soft" is not reassurance. Palpate deliberately with the patient performing a **Valsalva**, which can bring an impalpable node into reach.

SIDE GIVES THE NEXT CLUE

LEFT (Virchow node) drains via the **thoracic duct** → points at **abdominal, gastric or other GI malignancy**. **RIGHT** more often reflects **mediastinum, lung or esophagus**. So a left-sided node sends you to the abdomen and a right-sided one to the chest, before any imaging is ordered.

SIZE IS SITE-SPECIFIC

Generally **> 1 cm**, but applying that everywhere is wrong in both directions. **Epitrochlear > 0.5 cm is ALWAYS abnormal** (small, specific, easily skipped on exam). **Inguinal up to 1.5-2 cm is commonly NORMAL** in adults -the site most often over-investigated. **Any supraclavicular node is abnormal, whatever its size.**

FEATURES THAT SHIFT THE PROBABILITY

Feature	Reactive / benign	Malignant / serious
Consistency	**Soft, mobile, TENDER** -tenderness usually reflects rapid capsular stretch from inflammation	**Hard, rubbery, fixed or matted, PAINLESS. Stony-hard → carcinoma; rubbery → lymphoma**
Age	Under 40 -the great majority is benign	**Over 40 substantially raises risk**, and the threshold to biopsy falls with it
Duration	**< 2 weeks**, or **stable and unchanged beyond ~12 months** -both low-risk patterns	**Persistent > 4-6 weeks, or progressively enlarging**
Systemic	Preceding sore throat, dental infection, skin breach, viral prodrome	**B SYMPTOMS: fever, drenching night sweats, weight loss > 10% over 6 months.** Also pruritus, and rarely alcohol-induced nodal pain in Hodgkin
Elsewhere	Localized infection in the drainage territory	**Hepatosplenomegaly, cytopenias**, a breast or thyroid mass, or a skin lesion in the drainage area

LOCALIZED vs GENERALIZED · AND THE DRUG HISTORY

Pattern	What it means
Localized (one region)	**Examine the territory that node DRAINS** -see the regional map below
Generalized (≥ 2 non-contiguous regions)	Systemic causes: **EBV, CMV, HIV** (acute retroviral syndrome mimics mono -test broadly, not selectively), toxoplasma, **TB**, **syphilis**, lupus, RA, Still disease, **lymphoma and leukemia**, sarcoidosis. **Examine ALL nodal regions** -finding a second converts the workup
⚠ Drugs	**Phenytoin, carbamazepine, lamotrigine, allopurinol, sulfonamides** among others, sometimes as part of **DRESS**. A drug history costs nothing and occasionally ends the workup
Exposures to ask	**Cat scratch** (Bartonella), undercooked meat and cat litter (toxoplasma), **TB contact and country of origin**, ticks, animals, travel, **sexual history**, and **prior malignancy** -which reframes any new node as recurrence until proven otherwise

REGIONAL DRAINAGE: EXAMINE WHAT THE NODE DRAINS

Region	Drains	Think about
Cervical commonest overall	Scalp, ear, face, oral cavity, **teeth**, pharynx, thyroid	Viral URI, **streptococcal pharyngitis, EBV mononucleosis**, **dental abscess** (frequently missed -look in the mouth), **TB scrofula**, head and neck or thyroid malignancy. **Posterior cervical nodes favor EBV or toxoplasma**; anterior favors bacterial pharyngitis
⚠ Supraclavicular	**LEFT:** abdomen/thorax via thoracic duct. **RIGHT:** mediastinum, lung, esophagus	**MALIGNANCY until proven otherwise.** Gastric, pancreatic, ovarian, renal, testicular and lymphoma on the left; lung and esophageal on the right
Axillary	Arm, hand, chest wall, **breast**	**BREAST cancer -examine both breasts**. Also cat scratch disease and other hand or arm inoculation, sporotrichosis, and lymphoma. A unilateral axillary node in a woman is breast until excluded
Epitrochlear > 0.5 cm = always abnormal	Ulnar forearm and hand, 4th and 5th digits	Small and specific: **secondary SYPHILIS**, sarcoidosis, **lymphoma**, local hand infection. Easy to skip -palpate it deliberately
Inguinal 1.5-2 cm often normal	Lower limb, perineum, genitals, anus, lower abdominal wall	Usually benign, reactive to minor lower-limb trauma. But consider **STI** (syphilis, chancroid, lymphogranuloma venereum, herpes) and **anogenital, penile, vulval or cutaneous malignancy including melanoma**

TESTING, BIOPSY, AND TWO ERRORS THAT DELAY DIAGNOSIS

⚠ EXCISIONAL BIOPSY, NOT FNA

The most consequential procedural decision here. **Lymphoma classification requires tissue ARCHITECTURE together with immunophenotyping**, and FNA yields cells without architecture -so it is frequently non-diagnostic or misleading. **⚠ A "reactive" FNA does NOT exclude lymphoma**, and treating it as if it does is how diagnosis slips by months. **Excise the LARGEST and MOST ABNORMAL node, not the most accessible**, and **avoid inguinal** where possible since those so often show non-specific reactive change. **Alert the lab in advance** so tissue goes **fresh for flow cytometry** rather than straight into formalin. FNA is still reasonable for **suspected metastatic carcinoma or infection**, where architecture is not the question.

WORKUP & WHAT NOT TO DO

CBC with differential and film (atypical lymphocytes → viral; cytopenias or blasts → marrow, and the urgency changes), **LDH**, ESR/CRP, **HIV** plus targeted serology, and a **chest radiograph** for **mediastinal or hilar adenopathy** -often the finding that reframes everything toward lymphoma, sarcoid or TB. **Ultrasound** first for accessible nodes; **CT** for deep disease and staging. **⚠ NO empiric steroids before diagnosis** -they are lympholytic, can transiently shrink a lymphoma and falsely reassure, and can **obscure the histology enough to make the biopsy uninterpretable**. **⚠ No repeated empiric antibiotic courses** without a plausible source -that is just time passing. **If a biopsy is non-diagnostic but the node is still growing, repeat it.**

WHEN OBSERVATION IS REASONABLE

- **Observe 3-4 weeks** if: **under 40, localized, small, no red flags, plausible reactive cause.** Give **explicit return criteria** (growth, new nodes, fever, night sweats, weight loss) and **book the follow-up** rather than leaving it open.
- **⚠ Observation is NOT appropriate** for a **supraclavicular node**, any node with **B symptoms**, a **hard/fixed/matted** node, or one already present **beyond 4-6 weeks**. **Document size and character in NUMBERS**, or the follow-up visit is uninterpretable.

References: American Academy of Family Physicians reviews on the evaluation and differential diagnosis of unexplained lymphadenopathy · NCCN guidance on tissue sampling for initial lymphoma diagnosis · WHO classification requirements for lymphoma (architecture plus immunophenotyping) · published series on malignancy risk by nodal site and age.