Neack mass
• A new neck mass is a relatively common head and neck problem
• The mass may be the only manifestation of a serious and potentially malignant pathology, especially in the adult population.

• Evaluation of the neck mass must be approached in a thorough and disciplined manner.
• A thorough history and physical examination are essential first steps in the evaluation. This will narrow the diagnostic possibilities and help determine the appropriate next diagnostic steps.
APPROACH

• Our approach to evaluating a neck mass in adults relies upon findings on the initial history and physical examination to triage neck masses into three categories:
  • possible infectious
  • possible malignant,
  • possible nonmalignant
• And directs further evaluation with laboratory tests, imaging studies, tissue biopsies, and referrals accordingly.
Exclude or treat bacterial infection

- Infectious etiologies of a neck mass are suspected based on:
  - a history of the mass developing within a few days or weeks of an upper respiratory infection, dental infection, trauma, travel, or exposure to certain animals,

  or

- based on one of the following physical findings:
  - Warmth or erythema of the overlying skin, swelling or tenderness to palpation of the mass
  - Fever, tachycardia, or other systemic signs of infection
  - Rhinorrhea, odynophagia, otalgia, odontalgia, or other symptoms of a head and neck infection
Patients with a neck mass that appears to be infectious should be treated with a course of broad-spectrum antibiotics (eg, amoxicillin-clavulanate or clindamycin) and reevaluated in two weeks.

If the mass has completely resolved, the patient should be reevaluated in another two to four weeks for recurrence.

Patients who do not respond to or only partially respond to antibiotics, or who have recurrence after cessation of antibiotics, require further workup to exclude malignancy.
Most neck masses in adults are neoplastic rather than infectious.

Patients who do not have signs or symptoms suggestive of an infectious etiology should not receive antibiotics but instead undergo further workup.
Exclude malignancy

• Identification:

— A malignant neck mass should be suspected based on the following "stand-alone" features detected by the initial history and physical examination:

● History:

• Lack of an infectious etiology
• Duration of ≥2 weeks or unknown
• Age >40 years
• Tobacco or alcohol abuse
• History of head and neck cancer
• History of skin cancer of the scalp, face, or neck
• Immunocompromised status
Identification:

- Symptoms:
  - Hoarseness or recent voice change
  - Otalgia or recent hearing loss ipsilateral to the neck mass
  - Nasal congestion or epistaxis ipsilateral to the neck mass
  - Oral cavity or oropharyngeal ulcer
  - Odynophagia or dysphagia
  - Pharyngitis or "sore throat"
  - Hemoptysis or blood in saliva
  - Dyspnea
  - Unexplained weight loss
Identification:

- Physical examination:
  - Size >1.5 cm
  - Firm texture to palpation
  - Fixed or reduced mobility
  - Ulceration of overlying skin
  - Nontender neck mass
  - Asymmetric tonsils
  - Skin lesions on scalp, face, or neck
Evaluation

• Patients suspected of having a malignant neck mass based on the initial history and physical examination should:

• Be referred to a specialist (eg, otolaryngologist or ENT specialist) for a targeted head and neck examination in office or under anesthesia.

• Undergo a neck computed tomography (CT) or magnetic resonance imaging (MRI) with intravenous contrast. (See Imaging studies' below.)

• Undergo biopsy of the neck mass (typically a fine-needle aspiration but may require core or open biopsy). (See 'Diagnostic studies' below.)
Establish diagnosis

• Patients with a neck mass that is not infectious or at increased risk for malignancy require further testing to elucidate the etiology of the mass. These ancillary tests include laboratory tests (eg, for viral antibody titers) and a few selected imaging studies (eg, neck ultrasound for thyroid nodules or chest CT for tuberculosis or sarcoidosis). (See 'Laboratory studies' below and 'Imaging studies' below.)
PATIENT HISTORY
Age

- The age of the patient is a critical factor in the indicated diagnostic workup:
  - below 16: The majority of pediatric neck masses are either of inflammatory or congenital origin.
  - 16 to 40: Inflammatory or congenital etiologies also account for the majority of neck masses in the age group from 16 to 40, although the frequency of malignant causes start to increase.
  - >40: A neck mass in an adult over the age of 40 should be considered neoplastic, and potentially malignant, until proven otherwise.

- The probability of a malignant neck mass is further increased in the setting of tobacco or alcohol use.
Mass growth pattern

• Characteristics of the mass, such as its duration, growth pattern, and absence or presence of pain, are critical in making the diagnosis

➢ Masses that are present for years with little change are likely benign neoplasms (eg, benign salivary gland tumors, peripheral nerve sheath tumors, or paragangliomas).

➢ Rapidly expanding masses raise concern for infectious processes or rapidly growing lymphomas.

➢ Masses that fluctuate over time and increase with viral illnesses or upper respiratory tract infections are often congenital cysts.
Symptoms

• Pain is often related to rate of growth and expansion but can be related to direct neural invasion in the setting of certain malignancies. As an example, a fixed parotid mass that presents with pain is highly likely to be malignant.

• Symptoms of voice change, hoarseness, dysphagia, and otalgia may indicate cervical lymph node metastasis from an underlying upper aerodigestive tract malignancy.
Other history

A review of systems should include the presence of fever, night sweats, or weight loss. This constellation of symptoms is suspicious for lymphoma, whereas high, spiking fever suggests acute infection.

Important aspects of the social history include:
- tobacco use (frequency, total amount, method of use),
- alcohol use,
- illicit drug use (specially intravenous drug use),
- and HIV status.

An occupational history, occupational exposures, animal exposures, and recent travel history should also be included.
Other history

- Although smoking rates have decreased in the United States, with a consequent drop in the number of diagnosed oral cavity and laryngeal cancers, the incidence of human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC) has markedly increased. Patients with HPV-associated OPSCC have a distribution of demographic characteristics that is distinct from those with tobacco- or alcohol-related head and neck cancer.

  - Patients with HPV-associated OPSCC are most commonly White men, nonsmokers, and younger than 65 years and have few comorbidities. They are typically of high socioeconomic status and have risk factors for HPV exposure several decades prior to presentation.

  - Most importantly, in over two-thirds of cases, this disease will present as an asymptomatic neck mass. For this reason, there are often several barriers to timely and accurate diagnosis in these patients. For these reasons, it is imperative that patients with an asymptomatic neck mass undergo timely and thorough diagnostic workup along with prompt specialist referral when indicated.
COVID-19 vaccination

• The immunogenicity of the COVID-19 vaccine can lead to reactive cervical, axillary, or subpectoral adenopathy ipsilateral to the injection site. Abnormal nodal findings after the COVID-19 vaccine have been identified in 5 to 10 percent of patients, usually within two weeks of vaccination. Vaccine-related adenopathy often may be enlarged (>1 cm) with fluorodeoxyglucose (FDG) avidity. While such nodes will often demonstrate preserved morphology, reactive inflammation may also lead to loss of the fatty hilum. When biopsied, these nodes reveal reactive follicular hyperplasia.
• For these reasons, elective screening studies for head and neck cancer patients should be scheduled either before or at least six weeks after the COVID-19 vaccine to allow reactive adenopathy to resolve.

• When imaging must be obtained sooner, we recommend administering the vaccine contralateral to the patient's cancer when possible, with both doses given in the same arm.

• Most importantly, clear communication is essential between the patient, oncology team, and radiologist about the location and timing of the COVID-19 vaccine to ensure proper interpretation of imaging.
• Management of post-vaccination abnormal lymphadenopathy requires careful consideration of the clinical context. In most cases, vaccination history and nodal morphology is sufficient to rule out metastatic adenopathy.

• If there is high concern for potential disease involvement that would alter management, however, repeat imaging may be obtained in two weeks to assess for return to normal morphology. Alternatively, lymph node sampling may be performed.
PHYSICAL EXAMINATION

• The physical examination should include a careful evaluation of all anatomical areas that may be relevant to the neck mass.
Mass localization
Characteristics of the mass

- Palpation of the neck mass is critical, with attention to its:
  - location,
  - size,
  - shape,
  - consistency,
  - tenderness,
  - mobility,
  - and color
Neck masses due to "reactive" lymph nodes are usually discrete, mobile, firm or rubbery but not rock hard, and slightly tender.

Rock-hard, fixed masses raise concern for malignancy. Lymph nodes representing metastatic disease may be matted to the underlying structures and are usually nontender.

Infected lymph nodes are usually isolated, asymmetric, tender, warm, and erythematous; they may be fluctuant.

Soft, ballotable, mobile masses are often congenital cysts. However, in adults, cystic neck masses may represent nodal metastases from human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC).
• A rapidly expanding mass (over days to weeks) raises concern for infection or a rapidly growing lymphoma.

• A firm, lateral neck mass that moves from side to side but not up and down indicates involvement with the carotid sheath, such as a carotid body tumor or vagal schwannoma.

• A pulsatile quality or bruit suggests a vascular lesion.

• An immobile midline neck mass that elevates with swallowing indicates a thyroid source, such as a thyroglossal duct cyst or thyroid tumor.
Components of the general examination

• The oral cavity and oropharynx should be examined with thorough inspection of visible mucosa and bimanual palpation of the floor of the mouth and palpable portions of the tongue and neck.

• Examination of the ears may indicate a unilateral serous effusion related to nasopharyngeal carcinoma.

• A nasopharyngeal examination should be performed if there is no obvious etiology on oral and oropharyngeal examination; this usually requires a mirror examination and/or use of a flexible fiberoptic endoscope.
• A thorough examination of the skin of the head and neck can indicate a potential primary skin malignancy such as squamous cell carcinoma or melanoma.

• Assessment of cranial nerve function can suggest a neural tumor or ominous neural involvement by adjacent lymph nodes.

• A generalized skin rash may suggest a viral illness, whereas a localized skin lesion may indicate a more specific etiology (eg, cat scratch disease or tularemia).

• The thyroid gland should be carefully palpated and movement of the neck mass with swallowing noted.

• The position of the trachea should be evaluated for any deviation from midline.

• The abdominal examination should pay particular attention to possible enlargement of spleen or liver and presence of any masses.
LABORATORY STUDIES

• Laboratory evaluation should be initiated when the patient history or physical examination does not suggest transient reactive lymphadenopathy as the cause of a neck mass and can be performed simultaneously with a workup for malignancy in select patients.

• The extent of the laboratory evaluation will be determined by the potential differential diagnosis.
Most patients should have:
• Complete blood count (CBC) with differential

The following may be indicated for some patients:
• Erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) to evaluate for systemic inflammation or infection
• Blood culture (for febrile patients)
• Epstein-Barr virus (EBV) or Cytomegalovirus (CMV) serology (when adenopathy is diffuse)
• HIV serology (in patients with increased risk)
Specific serologic tests can be ordered when there is an increased index of suspicion for disease based on exposure, history, and examination:

- Serology for Toxoplasma gondii, brucellosis, Bartonella (cat scratch fever), tularemia
- Tuberculin skin test
- Antibodies to the Ro/SSA and La/SSB antigens, if Sjögren's disease is suspected as a cause of periparotid or submandibular masses

Abnormal test results may prompt additional evaluation, such as bone marrow biopsy if the CBC indicates possible hematologic malignancy.
IMAGING STUDIES

• Imaging studies offer specific details of anatomic position, mass consistency, adjoining involvement, vascularity, and potential primary source of malignancy in the region. Imaging options include ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and combined positron emission tomography (PET)/CT fusion scans.

• Contrast CT should be the initial study of choice for most adult patients with a neck mass

• Ultrasound evaluation of a neck lesion is more commonly used in Europe than in the United States (US).

• Greater experience has developed in the US for axial imaging by CT and MRI scanning. CT and MRI allow for the characterization of the mass and its relation to normal anatomic structures of the head and neck and may also help in identifying a primary source when metastatic disease is present.

• Angiographic imaging variants can be obtained with both study techniques (CT angiography or MR angiography), which may be helpful in evaluating masses of possible vascular origin.
Ultrasound

• The least invasive of the imaging techniques is ultrasound. Advantages of ultrasound include its noninvasive nature, real-time assessment of the mass and its relation to adjoining structures, and the ability to easily guide fine needle aspiration.

• Ultrasound is an excellent initial imaging modality for those at low risk of malignant disease, such as thyroid nodules without clinical evidence of extra thyroidal invasion or rapid growth.

• Ultrasound is also useful in those who wish to avoid the ionizing radiation of CT, such as in younger patients or those who require frequent surveillance imaging. Additionally, it is a relatively inexpensive imaging modality, with the current cost of a diagnostic neck ultrasound approximately $120
• There are several disadvantages to ultrasound, however, including: dependence on operator expertise and limited permanent images for use in consultant evaluation or the operative setting.

• Interobserver reliability in neck ultrasound is variably reported in the literature and focuses largely on the interpretation of thyroid nodules.

✓ In an evaluation of 365 patients with clinically suspected thyroid lesions all separately scanned by six ultrasonographers, interobserver reliability was excellent and increased with experience of the observer.

✓ Not all studies, however, have shown such a high degree of interobserver agreement, particularly in nodule margin and echogenicity.

❖ Caution should be used when making conclusions about changes in the size or character of a mass over time, especially with interfacility ultrasound comparison, as different ultrasound systems may produce significant differences in image quality and interpretation.
Computed tomography

CT is:

• well tolerated by patients,

• and reformatting algorithms allow evaluations in all relevant planes.

• It also yields excellent bone detail and is the study of choice for neck masses arising from or adjacent to bony structures.

• Image acquisition is fast,

• and the cost of CT is not substantially higher than that of ultrasound, with the price of contrast enhanced neck CT approximately $240.

• It is an excellent initial diagnostic study in patients at higher risk of malignancy or those with possible involvement of deep neck spaces, particularly those poorly visualized by ultrasound, including parapharyngeal and masseteric spaces.
• A limitation of the CT scan is its use of ionizing radiation.

✓ A typical head and neck CT imparts a radiation dose of approximately 4 mSv. However, annual background radiation from natural sources in the US is approximately 3 mSv. In that way, a single CT scan has a negligible effect on a patient's lifetime incidence of developing malignancy.

✓ Consideration of the ionizing effects of CT scanning should only affect management decisions in pediatric patients, who may be at an increased risk of radiation-induced malignancy, and in patients undergoing very frequent surveillance imaging.
Magnetic resonance imaging

— MRI is indicated for:

• masses that require further definition of soft tissue
  ✓ infiltrative soft tissue masses,
  ✓ suspicion of malignant perineural spread,
  ✓ or potential central nervous system origin.
Advantages of MRI include:

✓ outstanding soft tissue differentiation,
✓ lack of ionizing radiation,
✓ and infrequent contrast allergy.

CT vs MRI

Imaging acquisition for MRI takes longer than CT and may be challenging for claustrophobic patients. MRI is also more expensive than both ultrasound and CT, with the price of a contrast-enhanced orbits/face/neck MRI approximately $420.
Positron emission tomography

PET/CT fusion scans have been found useful in the setting of malignancy, aiding in the identification of primary disease, or detection of distant metastatic disease.

• PET/CT is primarily helpful in the later evaluation of malignancies and plays little role in the initial evaluation of the neck mass.

PET/CT scanning does impart a significantly high equivalent radiation dose, which may be as high as 32 mSv and, with frequent scanning, may appreciably increase the lifetime attributable risk of malignancy.
DIAGNOSTIC STUDIES
Fine-needle aspiration

- Fine-needle aspiration (FNA) is the preferred diagnostic approach for most neck masses and is typically performed using a 25 or 27 gauge needle on a 20 mL syringe.
- The nature of the aspirate may suggest particular etiologies:
  - Blood (vascular lesion)
  - Serous dark brown fluid (papillary thyroid cancer)
  - Thick viscous yellow fluid (mucocele)
  - Turbid yellow fluid (branchial cleft cyst)
  - Purulent (abscess)
• Whether performed in the office or a radiology suite, on-site evaluation of FNA samples by trained cytopathologists results in the lowest rate of sample inadequacy (6 versus >10 percent).

• The initial cytopathological analysis of FNA is by smear preparation, which may be limited by blood products, hypocellularity, and variable smear thickness.
• The addition of cell block preparation to standard cytopathological analysis has been shown to reduce the rate of unsatisfactory samples and improve diagnostic accuracy.

✓ Cell blocks are prepared by centrifugation of material obtained through FNA, which can then be sectioned for further pathological analysis, including immunohistochemical staining.

✓ This can be especially useful in certain pathologies, including lymphoma and human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC).
• In particular, FNA is an important initial diagnostic tool in patients at risk for lymphoma. Even if initial needle biopsy is unable to provide exact subtype definition, FNA can quickly rule out carcinoma or other pathology in these patients and identify those who would benefit from excisional biopsy.

• Besides cytologic analysis, FNA aspirate can also be submitted for polymerase chain reaction (PCR) testing for virus such as the presence of Epstein-Barr virus (EBV), which can suggest the diagnosis of a nasopharyngeal carcinoma, or HPV, which has been implicated in OPSCC.
• FNA is a safe, highly accurate diagnostic procedure but is dependent upon the skills of the clinician performing the procedure to avoid sampling errors and the accuracy of cytopathological interpretation.

• A meta-analysis found an overall accuracy of 93 percent (ranged 73 to 98 percent) for FNA in diagnosing all neck masses regardless of location or histology
The isolated lateral neck cyst in an adult, however, remains a diagnostic challenge. As discussed above, in patients over 40 years, lateral neck cysts may represent cervical metastasis from HPV-associated OPSCC. In these masses, the cyst lining is often the only diagnostic component, which decreases the specificity of FNA, especially that performed without image guidance. In a review of 121 lateral neck cysts, metastatic squamous cell carcinoma was identified in 24 percent of patients over 40 years.

However, of patients who underwent preoperative FNA, over 30 percent with negative FNA results were subsequently found to have malignant pathology after cyst excision.

✓ For this reason, the treating clinician must maintain a high degree of suspicion in older adult patients with isolated neck cysts despite a negative FNA.

Analysis of cyst fluid for HPV DNA and the use of cell block analysis may improve diagnostic accuracy in cases of occult HPV-associated OPSCC.
Core biopsy

• If the information provided by an FNA does not establish the diagnosis, core needle biopsy can be considered.

• Core biopsies in the head and neck are generally performed under local anesthesia with a 14 to 20 gauge cutting needle. One to five passes are typically performed with an automatic needle gun for precise tissue acquisition.

• Advantages of core biopsy include:
  - greater tissue yield,
  - leading to lower rates of nondiagnostic samples;
  - decreased variability in pathological interpretation;
  - and improved diagnostic accuracy in specific disease processes that require analysis of tissue architecture or flow cytometry, such as lymphoma.

  ✓ In a review of 237 patients who underwent core needle biopsy in the workup of lymphoma, 97 percent were fully diagnostic, allowing treatment initiation without excisional node biopsy.
The disadvantages of core biopsy are:

- primarily related to the potential trauma from larger-bore needles.
- tumor seeding

Although increasing needle size may theoretically increase the risk of nerve injury or tumor seeding, in practice these events are exceedingly rare and do not appear more frequently for core biopsy than FNA.

In a systematic review of the literature including 610 articles, the estimated rates of tumor seeding after either FNA or core biopsy were below 0.002 percent
Image-guided biopsy

- Ultrasound-guided or CT-guided FNA or core biopsies are considered in the setting of nonpalpable masses seen only with imaging.

- Advantages of image guidance include: precise sampling adjacent to critical neurovascular structures as well as the ability to target higher-yield areas within a complex cystic-solid lesion.

- A randomized trial involving 81 patients with a head and neck mass less than 3 cm demonstrated improved tissue adequacy for FNA using ultrasound guidance as compared with palpation alone [Robitschek J, Straub M, Wirtz E, et al. Diagnostic efficacy of surgeon-performed ultrasound-guided fine needle aspiration: a randomized controlled trial. Otolaryngol Head Neck Surg 2010; 142:306].

- Most neck masses within 3 cm of the skin surface are amenable to ultrasound guidance. CT procedures are used for deeper lesions or those without an echogenic window, such as high neck masses under the mandible.
Excisional or incisional biopsy

• Open surgical biopsies, in general, are discouraged since they can adversely affect the success of subsequent definitive treatment in malignant pathologies and in certain situations, even for benign disease, may lead to disastrous results:
  • Open biopsy of paragangliomas of the head and neck could result in life-threatening hemorrhagic complications
  • Open biopsy of schwannomas, including those arising from the vagal or facial nerves, may result in permanent and unexpected nerve deficits.
  • Periparotid masses may represent salivary gland neoplasms, and open biopsy may increase the risk of tumor recurrence and increase the technical difficulty of subsequent definitive resection.
• For excisional node biopsies that are found to be metastatic squamous cell carcinoma, the ultimate impact of open biopsy on oncologic control remains controversial. However, surgical excisional or incisional biopsy of a neck lesion that is subsequently found to be malignant creates several challenges for both the patient and treating clinicians. If definitive surgery is later performed, completion lymph node dissection is substantially more difficult in the setting of prior surgery. In addition, open biopsy risks tumor spillage and requires resection of prior incisions and surrounding scar or may require higher radiotherapy dosing to the prior surgical bed when definitive nonsurgical treatment is delivered [65].
• Open biopsy can be more acceptable in the setting of an FNA or core biopsy being positive for lymphoma, but additional tissue is necessary for subtyping.
If open resection of a cystic neck mass with benign or nondiagnostic FNA results is considered, referral must be made to a provider capable of performing completion node dissection in the same setting should the diagnosis return intraoperatively as a malignant head and neck cancer. This is particularly relevant in the HPV-associated OPSCC era where young nonsmokers with few comorbidities may present with cystic neck lesions initially mistaken for congenital cysts. As discussed above, needle biopsy of these masses is often nondiagnostic or falsely negative given their cystic nature, and a high level of suspicion must be maintained in these patients [20]. (See 'Other history' above and "Epidemiology, staging, and clinical presentation of human papillomavirus associated head and neck cancer", section on 'Treatment'.)