1. ORBITAL DISEASE WORK-UP

a. History

1) Pain - inflammation/infection/ consider orbital cellulitis/IOIS
2) Progression - fast: Rabdomyosarcoma/infection/ consider orbital cellulitis vs young male (rabdo)
3) Proptosis - location of mass (opposite of proptosis)/ lacrimal gland tumor (down/in)
4) Palpation - anterior orbit location/ consider dermoid/newborn/infant
5) Pulsation - vascular: consider arteriovenous fistulas/ recent head trauma
6) Periorbital changes - "strawberry patch" – consider capillary hemangioma/ young female

b. Ocular/Physical Exam & Testing

1) Inspection
2) Palpation
3) Auscultation
4) Exophthalmometry – norm values

c. Special Testing & Imaging

1) Orbital X-rays - detect orbital / intraocular foreign body
2) Ultrasonography
   a. A-scan
   b. B-scan
   c. Doppler
3) CAT scan
4) MRI
5) Venography
6) Arteriography
7) MRA imaging

d. CLINICAL PEARLS

• It is important to establish with history and ocular/physical examinations a narrow differential diagnosis that can be used to plan the initial course of management.
2. PEDIATRIC DISORDERS

a. Infectious (Orbital Cellulitis)

1) Epidemiology – incidence
Orbital cellulitis has an approximate incidence of 3 to 6/1,000,000. It has a higher incidence in blacks than in whites or Hispanics and is slightly more common in men than in women. Finally, it is more common in children than in teenagers and adults.

2) Risk factors
• Sinusitis
• Periocular trauma

3) History
Patient presents acutely with increasing edema, erythema, and pain around the eye that has occurred over several hours to several days. Many will have a history of underlying sinus disease, an acute respiratory tract infection, skin infection, or recent trauma. They progress to develop decreased motility with double vision (if the eyelids are not swollen shut).

4) Physical exam
• Erythema and edema of lids and orbit
• Proptosis
• Decreased vision
• Conjunctival injection and chemosis
• Limitation in ocular motility
• Sluggish pupil with possible afferent pupil defect
• Elevate intraocular pressure

5) Diagnostic tests and interpretation
Lab
• CBC with white count
• Culture of any discharge
• Blood cultures may be helpful

Imaging
Initial Approach
• CT scan of the orbits

6) Medication
First Line
Broad-spectrum IV antibiotics that cover gram positive, gram negative, and anaerobes, especially in patients older than 14 years. These include fortified penicillins, third-generation cephalosporins, fluoroquinolones, or a combination of these medications. Intravenous antibiotic choices would include ampicillin sulbactam, ceftriaxone, aminoglycosides, vancomycin, clindamycin, and fluoroquinolones.
7) CLINICAL PEARLS

- It is important to consider MRSA as a cause of infection when choosing appropriate antibiotic therapy.
- CT scan of the orbit and sinus is a very helpful tool when determining the best course of treatment.
- Antibiotics are most effective as single therapy in young children, whereas antibiotics and surgery are more often needed in teenagers and adults.

b. Cysts & Teratomas (Dermoids and Epidermoids)

1) Incidence

- Orbital dermoid/epidermoid cysts
  - Incidence – most common space-occupying orbital lesion of childhood. May comprise 30-46% of excised orbital tumors in children.
  - Age at diagnosis is most commonly in infants and young children, but may be diagnosed at any age
  - Sex – no predilection
- Teratomas – most commonly found in gonadal tissue, rarely involves the orbit
- Incidence – very rare in the orbit
- Age – majority present at or shortly after birth
- Sex – 2:1 Females:Males

2) History

- Orbital dermoid/epidermoid cysts
  - Generally asymptomatic unless they increase in size or rupture (spontaneously or with trauma) resulting in an inflammatory reaction and pain
  - Rarely cause proptosis or displacement of the globe
  - Growth of these lesions is typically slow
- Orbital teratomas
  - Rapidly growing proptosis noted at birth or early infancy
  - Typically unilateral

3) Physical Exam

- Orbital dermoid/epidermoid cysts
  - Frequently presents as painless, subcutaneous mass
  - Typically located in the superotemporal orbital region (frontozygomatic suture), less frequently superonasally
  - On palpation are not fixed to overlying skin – they are partially mobile, smooth, and not tender to touch
  - Do not affect vision or intraocular pressure

3) Diagnostic Tests & Interpretation

Imaging

- Orbital dermoid-epidermoid cysts
- Initial approach
o Orbital CT (with axial and coronal views) or MRI to aid with surgical planning
  o On CT – a round to ovoid lesion with distinct margins. Lumen is usually homogenous and does not enhance with contrast.

4) Treatment
   Issues for referral
   • Orbital dermoid/epidermoid cysts
     o If asymptomatic, patient may follow-up routinely with an optometrist or pediatric ophthalmologist
     o If large or symptomatic (globe displacement, pain, inflamed), consider referring promptly to an oculoplastics surgeon or pediatric ophthalmologist

5) CLINICAL PEARLS
   • Both orbital dermoid/epidermoid cysts and orbital teratomas are typically benign lesions.
   • Orbital dermoids/epidermoids are usually superotemporal, painless subcutaneous masses that do not commonly affect vision or intraocular pressure.

c. Benign Harmatomas (Capillary Hemangiomas)
   Some believe that capillary hemangiomas (CHs) could represent placental “metastasis.”

1) The most common benign tumor in pediatric population affect up to 2% of all infants.
   • F:M ratio 3:1-2
   • Multiple gestations and preterm infants have a higher rate (25%) of Cutaneous lesions
   • Incidence of periocular CH is approximately 1/10 that of systemic IH
   • 60% occur in the head/neck area and 20% have > 1 IH (infantile hemangioma)
   • Account for 5.6% of all pediatric orbital tumors

2) Risk factors
   • Prematurity
   • Multiple gestation
   • Advanced maternal age of greater than 30 years
   • Low birth weight
   • Maternal chorionic villus sampling or amniocentesis

3) History
   • 2% of IHs are present at birth; the majority become evident in the first few postnatal weeks.
   • Typically described by the parents as a small pink scratch that enlarges and may become a protruding mass
This differs from a port-wine stain in Sturge-Weber syndrome, which is present at birth, occurs in the V1 distribution, and does not typically produce mass effect and does not blanch with applied pressure.

- Timing of involution:
  - 30% involute by age 2 years
  - 60% involute by age 4 years
  - 76% involute by age 7 years

4) Physical Exam
   - Superficial IHs display classic strawberry red pigmentation that blanch with pressure.
   - Deep hemangiomas may have a bluish hue
   - Lesions are soft and compressible
   - May expand when head is held in a dependent position, with crying, or Valsalva
   - IH often present at multiple levels

5) Diagnostic tests & interpretations
   - Imaging
     - Gadolinium-enhanced MRI demonstrates extent of orbital lesions
     - Black serpiginous signal voids on T1- and T2-weighted images secondary to high flow rate. T1 lesions is isointense with the brain; T2 lesions is hyperintense.
   - CT
     - Diffuse homogeneous soft tissue mass with marked enhancement with contrast

6) Treatment Indications
   - Decision to treat periocular hemangiomas is directed by four factors:
     - Location
     - Extent
     - Degree of or potential for amblyopia
     - Presence of systemic hemangiomas
   - First line
     - Propranolol, oral: 2 mg/kg/day divided in 3 doses. This is a new, evolving treatment for select cases
     - Some advise starting at 0.5 mg/kg/day for 1 week, then 1 mg/kg/day for 1 week if tolerated then maximal dose at 2 to 3 mg/kg/day. If monitoring as inpatient, can increase dose 0.5 mg/kg/day daily to reach maximum dose.

7) CLINICAL PEARLS
   - Benign superficial or deep vascular hamartoma
   - Potential for amblyopia and/or strabismus
   - Treat if amblyopia present or likely, systemic hemangiomas, or large
   - Treatments include beta-blockers, steroids, or surgery
d. Infiltrative lesion (*Optic Nerve Glioma*)

1) Description
   - Most common infiltrative lesions of the optic nerve (ON)

2) Epidemiology
   **Incidence**
   - 1% of all intracranial tumors
   - 3% of orbital tumors
   - 4% of all gliomas
   - Occurs in 15% of patients with NF1
   - Represents 65% of intrinsic optic nerve tumors
   - 90% recognized by second decade of life
   - Also known as optic pathway glioma (OPG)

3) Risk factors
   - Neurofibromatosis type 1 (NF1) in 25-30% of cases of OPG

   **Genetics**
   - Localized to chromosome 17 if associated with NF1 (autosomal dominant)

4) History
   - Progressive painless visual loss +/- proptosis and/or diplopia
   - History of NF1

5) Physical exam
   - Demonstrates features of an optic neuropathy: Decreased visual acuity, decreased color vision, nerve fiber bundle-type visual field defects though may have temporal defects of homonymous defect if concurrent involvement of the optic chiasm or tract respectively, afferent papillary defect if unilateral or asymmetric optic nerve involvement
   - Optic nerve may be pale or edematous based upon location of tumor with anterior involvement producing ON edema while posterior orbital, canalicular, or intracranial lesions demonstrate ON pallor
   - May have proptosis, strabismus, or nystagmus
   - May have stigmata of NF1 (e.g., Lisch nodules, café au lait spots, dermal neurofibromas)

6) Diagnostic tests & interpretation
   **Imaging**
   **Initial approach**
   - MRI brain and orbits with and without contrast including T1 post-contrast images with fat suppression
     - MRI demonstrating characteristic features generally sufficient to establish diagnosis
Fusiform or occasionally diffuse enlargement of the intraorbital optic nerve
- Intense enhancement common
- “Kinking” of the optic nerve within the orbit
- “Pseudo-CSF” signal on T2 images secondary to perineural arachnoidal gliomatosis in patients with NF1

7) Medication

First Line
- Observation without treatment unless clear evidence of progression with extension into the chiasm, opposite ON, or hypothalamus
- Chemotherapy reserved for patients <6 years old

8) CLINICAL PEARLS

- Characteristic ON “kinking” on MRI is almost exclusively seen in NF1
- Relatively high incidence of NF1 in patients with OPG

e. Neoplasms (*Rhabdomyosarcomas*)

1) Description

- Rhabdomyosarcoma (RMS) is a highly malignant neoplasm that arises from pluripotential cells that demonstrate histopathologic features of striated muscle

2) Epidemiology

**Incidence**
- 4.3 cases per 1 million children for all cases of RMS
- 5:3 male to female ratio for RMS of the orbit
- No racial predilection

3) Risk factors

- Maternal use of marijuana during pregnancy has been found to cause 3-fold increased risk
- Maternal use of cocaine during pregnancy is associated with 5-fold increased risk
- Paternal use of marijuana, cocaine, or any recreational drug is associated with 2-fold increased risk

4) History

Based on a large review of orbital RMS by Shields et al., the history reveals:
- Mean age at presentation of 10 years
- Acute and subacute painless proptosis in 30%
- Eyelid swelling in 21%
- Conjunctival injection in 9% and edema of the eyelids in 21%
- Symptoms present for a mean of 5 weeks
- Downward and outward displacement of the globe
- Pain and decreased vision are uncommon
- History of trauma
5) Physical exam
Based on a large review of orbital RMS by Shields et al., the history reveals:
- Orbital mass in 76%
- Conjunctival mass in 12%
- Proptosis in 79%
- Chemosis in 41%
- Eyelid edema in 21%
- Can mimic inflammation

6) Diagnostic tests & interpretation
   **Lab**
   Initial lab tests
   - CBC count with differential to rule out leukemia, infection, and other simulating conditions

   **Imaging**
   Initial approach
   - MRI of orbits
   - CT of orbits
     - Round, oval, or irregular mass
     - Well-circumscribed or diffuse

7) Medication
   **First Line**
   Chemotherapy is delivered by a pediatric oncologist. According to the Intergroup Rhabdomyosarcoma Study Group.

8) CLINICAL PEARLS
   - Presentation can mimic inflammation/trauma.
   - Remove lesion completely if possible.
   - Adjuvant chemotherapy and radiation has improved survival to 95%.

3. ADULT DISORDERS
   a. Vascular (**Cavernous Hemangioma**)
      1) Description
         - Cavernous hemangioma of the orbit is a benign proliferation of vascular channels which induces progressive ectasia
      2) Epidemiology
         **Incidence**
         - Estimated 4-12% of orbital tumors – the most common orbital tumor in adults
         - Rarely occurs in infants or children
         - Female > male
3) History
- Painless, progressive proptosis
- Hyperopic shift in refraction
- Pressure sensation
- Diplopia
- If advanced, vision loss due to optic neuropathy
- Often discovered on imaging for other reasons, i.e., headache

4) Physical exam
- Hertel exophthalmometry for baseline and comparison
- Resistance to retropulsion
- Dilated episcleral vessels
- Choroidal folds on funduscopic exam due to compression of globe
- Evaluate for compressive optic neuropathy:
  - Relative afferent papillary defect
  - Vision loss
  - Color testing
  - Visual field testing
  - Optic nerve edema or atrophy

5) Diagnostic tests & interpretation
   Imaging of orbits – CT/MRI (intraconal mass)

6) Treatment
   - Surgical resection (orbitotomy) if compression of optic nerve, extraocular muscles, or the globe is evident. Surgery may also be indicated for severe proptosis or for pathologic diagnosis if the identity of the mass is in question.

b. Carotid Cavernous Fistula (CCF high flow/CCF low flow)

1) Description
   A carotid/cavernous sinus fistula (CCF) is an abnormal communication between an artery and the venous plexus within the cavernous sinus (CS). This can occur spontaneously or secondary to trauma. Fistulas are broadly categorized based on the flow rate (high or low) and more specifically by the feeder vessel(s)

<table>
<thead>
<tr>
<th>The Barrow classification of CCF</th>
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<tbody>
<tr>
<td><strong>Type</strong></td>
</tr>
<tr>
<td>A</td>
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<td>ICA = internal carotid artery; ECA – external carotid artery</td>
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2) Risk factors
- Hypertension
- Atherosclerosis
- Collagen vascular disease
- Connective tissue disease (Ehlers-Danios)
- Pregnancy
- History of carotid artery aneurysm
- History of trauma

3) History
- Presenting symptoms vary widely and depend on the amount of blood flow through the fistula. High-flow fistulas can present with marked proptosis, diplopia, and decreased vision. Low-flow fistulas may only have mild conjunctival injection.
- The patient may have a recent or distant history of trauma, which may or may not have affected the head.
- Complaints of a dull retrobulbar ache or “whooshing” sound in the head may be present.
- In lower flow lesions, the patient’s only complaint may be of a unilateral or, less frequently, bilateral red eye of varying duration, from days to months. Patients may have seen multiple physicians and carry a variety of misdiagnoses, including conjunctivitis, allergic reaction, dry eye.
- Some patients may elicit a history of unilateral glaucoma, often diagnosed at the time of the red eye.

4) Physical Exam
- Decreased vision, dyschromatopsia, and afferent papillary defect: Usually secondary to vascular compromise of the optic nerve or retina
- Asymmetrically elevated intraocular pressure: Secondary to decreased episcleral venous outflow into a congested orbit
- Conjunctival injection: As the CS becomes arterialized with blood from the feeding vessel(s), the venous outflow of the orbit becomes congested, causing the conjunctival vessels to become dilated and tortuous. At the slit lamp, “corkscrewing” of the conjunctival vessels extending to the limbus may be present.
- Proptosis: As orbital venous congestion develops, the globe becomes anteriorly displaced
- Bruit: A supraorbital bruit may be auscultated in higher flow lesions
- Optic nerve edema

5) Diagnostic tests & Interpretation

**Imaging**

Initial approach
- Orbital color Doppler ultrasonography: A noninvasive method to detect an enlarged SOV with reversal of flow and an arterialized waveform. The sensitivity and specificity of this test is unknown, but is probably more reliable in higher flow states.
• CT-CTA: In cases where trauma is involved, this is usually the first imaging study done. Typical findings include an enlarged superior ophthalmic vein (SOV), thickened extraocular muscles and an enlarged CS. The sensitivity of CTA is dependent on the caliber of the fistula.
• MRI/MRA: Similar findings as in CT. MRI may also show slow flow or thrombus formation within the SOV.
• Angiography: This is the gold standard, can diagnose small arterial feeders, and allows simultaneous management by embolization. It is important to perform angiography of the entire cranial arterial system (“six vessel” angiography).

6) Treatment
General Measures
Low-flow fistulas with few clinical manifestations can be observed and may close spontaneously. Carotid massage is an effective measure for the closure of low-flow lesions. The patient is instructed to always use the contralateral hand to perform the massage to minimize the risk of permanent ischemic injury to the brain.

Issues for Referral
• Because of the ocular manifestations, it is common for an optometrist/ophthalmologist to make the initial diagnosis. All CCFs should be referred to a neurosurgeon or interventional neuroradiologist for angiography and treatment.
• Timing of referral is important. Chronic symptomatology is less urgent than more acute manifestations. In acute lesions, the possibility of posterior cortical venous outflow with the attendant risk of hemorrhagic stroke must be considered.

7) CLINICAL PEARLS
• Indirect, low-flow fistulas can be difficult to diagnose clinically. In chronic cases where there is no threat to the vision close observation is acceptable, as spontaneous resolution may occur.
• Permanent visual loss may occur from CCFs.
• Posterior cortical venous outflow in CCF increases the risk of hemorrhagic stroke.

c. Neoplasms (**Lacrimal Gland Tumor**)

1) History
• Careful history must be taken regarding previous malignancies, lacrimal gland biopsies, or surgeries
• Epithelial and nonepithelial malignancies: Inferior and nasal globe displacement with proptosis. Lesions are typically painless, although pain may be seen with bony erosion or perineural involvement (typical of adenoid cystic carcinoma).
• Benign epithelial tumors: Typically a long history of painless proptosis ± globe displacement. “S-shaped” proptosis seen in orbital lobe involvement.

2) Physical Exam
• Physical exam should be a thorough ophthalmological evaluation with consideration of all aforementioned potential etiologies.
• Visual acuity, intraocular pressure, visual fields and extraocular motility should be evaluated in all patients.
• All cranial nerves should be evaluated, and the presence or absence of ptosis should be documented.
• Optic nerve involvement and infiltration should be evaluated with visual fields, color plates, and papillary examination.

3) Diagnostic tests & Interpretation
   Imaging
   • Orbital CT with axial and coronal views. Look at the lacrimal gland fossa (superotemporal orbit) for the presence of any bony erosion.
   • MRI if suspicion of intracranial extension
   • Chest x-ray to evaluate for sarcoidosis, tuberculosis, primary malignancy, or metastases

4) Treatment
• Adenoid cystic carcinoma and other epithelial malignancies: Orbital exenteration is usually indicated, particularly in adenoid cystic carcinoma.

   d. Metastatic (Orbital Breast and Lung Metastatic Disease)

   1) Pathophysiology
   • Extraocular muscles are often seeded because of their abundant blood supply.
   • The bone marrow of the sphenoid bone is also commonly involved because of the high volume of low-flow venous channels in the bone.

   2) History
   • Average age of presentation is seventh decade in adult cases.
   • 25-35% of patients do not have a primary malignancy at the time of ocular presentation.
   • Diplopia, pain, and visual loss are most common symptoms.
   • Also, ptosis (droopy eyelid), proptosis (bulging eye), eyelid swelling, and palpable mass are common features.
3) Physical exam
   • Clinical presentation can be divided into 3 subcategories:
     o Infiltrative is characterized by motility restriction, resistance to retropulsion, ptosis, and enophthalmos.
     o Mass is characterized by proptosis and often a palpable orbital mass.
     o Inflammatory is characterized by pain, chemosis, erythema, and periorbital swelling.
   • Decreased vision can occur from orbital congestion, with optic neuropathy and choroidal folds.
   • Enophthalmos is another important diagnostic sign. It comes from tethering and posterior traction on the globe from scirrhou s metastasis such as breast or gastrointestinal carcinoma.

4) Diagnostic Tests & Interpretation
   **Lab**
   Patients suspected of having metastatic disease by history and examination should have biopsy before extensive lab testing is performed.

   **Imaging**
   CT scan or MRI with contrast can delineate extent of orbital involvement. These images may assist in surgical planning.

5) Medication
   Medical treatment, that is, chemotherapy and hormone therapy, varies depending upon the type of primary neoplasm and its stage. External beam radiotherapy if often used as additional therapy.

6) Additional treatment
   **General Measures**
   • Treatment is aimed at preserving vision and addressing pain
   • External beam radiotherapy is often first line treatment for local control of orbital tumor

7) CLINICAL PEARLS
   • A quarter of all patients with orbital metastasis do not have a primary diagnoses at the time of presentation.
   • An ophthalmologist or optometrist may therefore be the first to diagnose a serious illness like metastatic cancer. A high index of suspicion and rapid diagnosis is crucial. Prompt referral for systemic work-up can then be pursued.
   • Enophthalmos can be the tricky presenting sign of scirrhou s breast carcinoma or gastrointestinal cancer. It is often confused with contralateral proptosis.