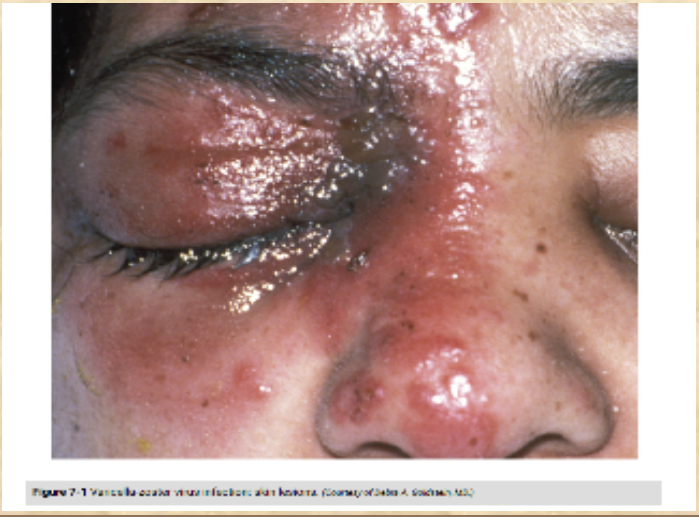
Decreased Vison Secondary to Uveitis



Uveitis and Systemic Disease

Uveitis can be defined as inflammation of the uvea, the middle, vascular coat of the eye *(Greek uva- grape)* The uvea consists of the iris, ciliary body and the choroid. The International Uveitis Study Group classification separates uveitis anatomically by location of observed disease according to visible signs- anterior posterior or intermediate. Iritis is a synonym for anterior uveitis..

Uveitis

- Uveitis, a term correctly used to describe inflammation of the uveal tract (iris, ciliary body, choroid) alone, in reality comprises a large group of diverse diseases affecting not only the uvea but also the retina, optic nerve and vitreous. Uveitis is a major cause of severe visual impairment and has been estimated to account for 10-15% of all cases of total blindness in the USA. In surveys of the causes of blindness uveitis has usually not been included and is probably

Uveitis and Systemic Disease

International Classification of Uveitis

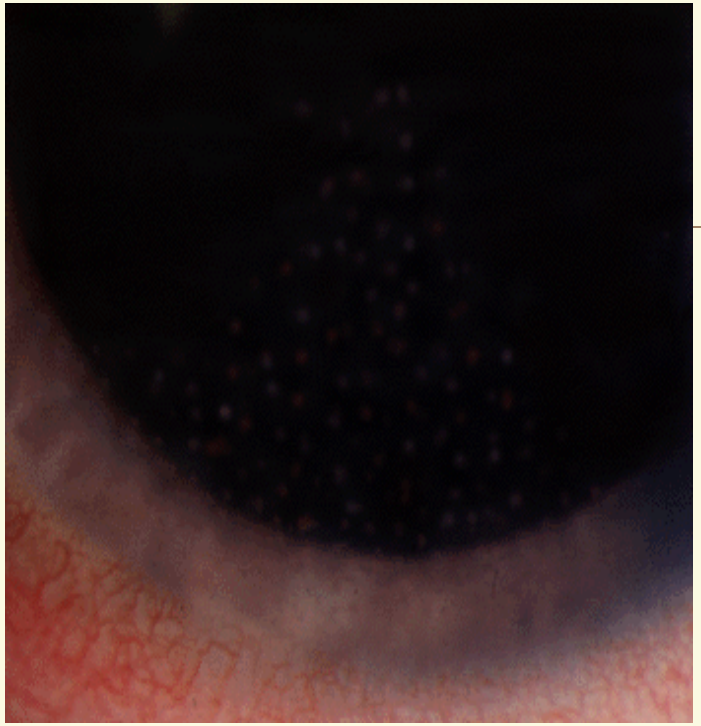
Temporal- Acute versus Chronic (>3 months)
In acute uveitis symptoms and signs occur suddenly and typically lasts up to 6 weeks. In chronic uveitis the onset is usually gradual and the inflammation lasts longer than three months.

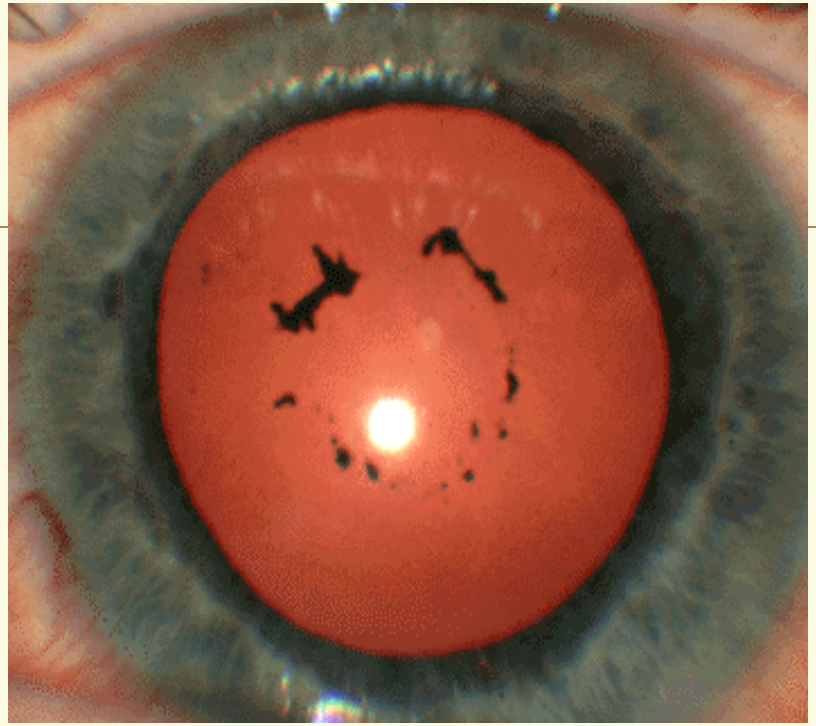
Anatomical

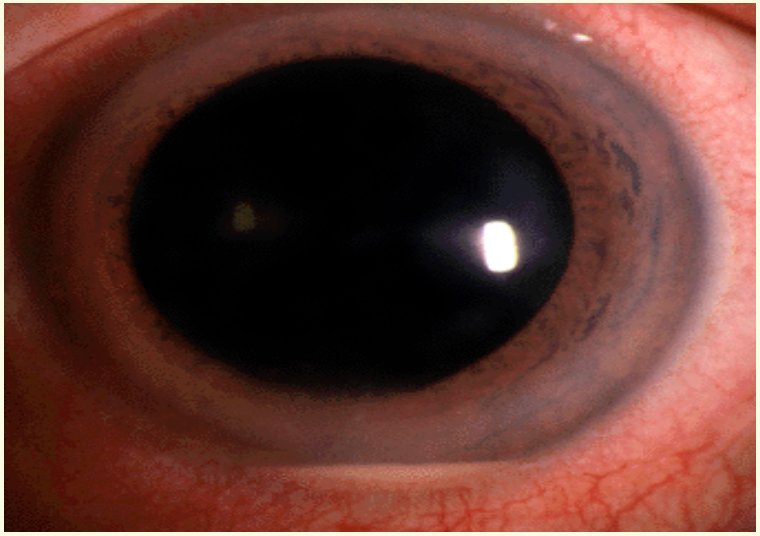
Anterior Uveitis (Iris and anterior ciliary body)

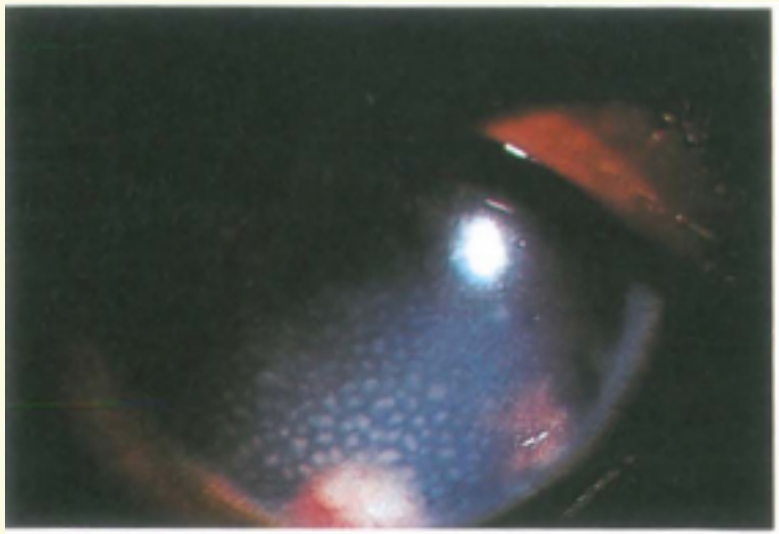
Intermediate Uveitis (posterior ciliary body- pars plana)

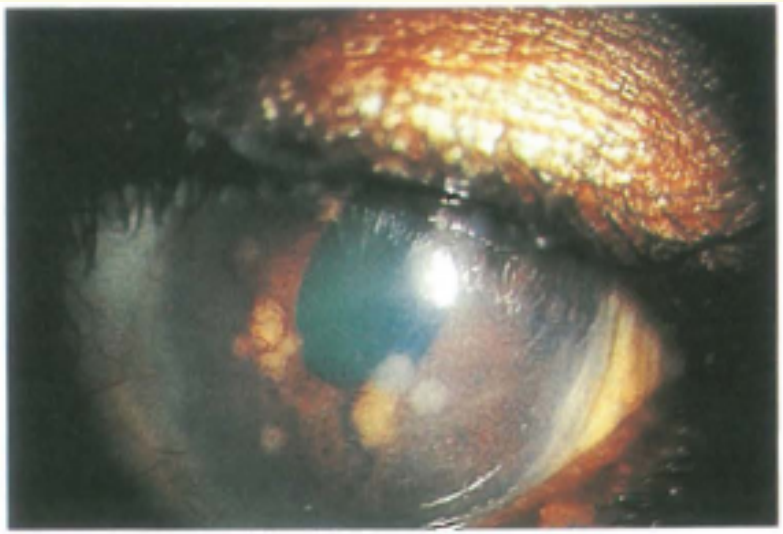
Posterior Uveitis (predominantly choroid)

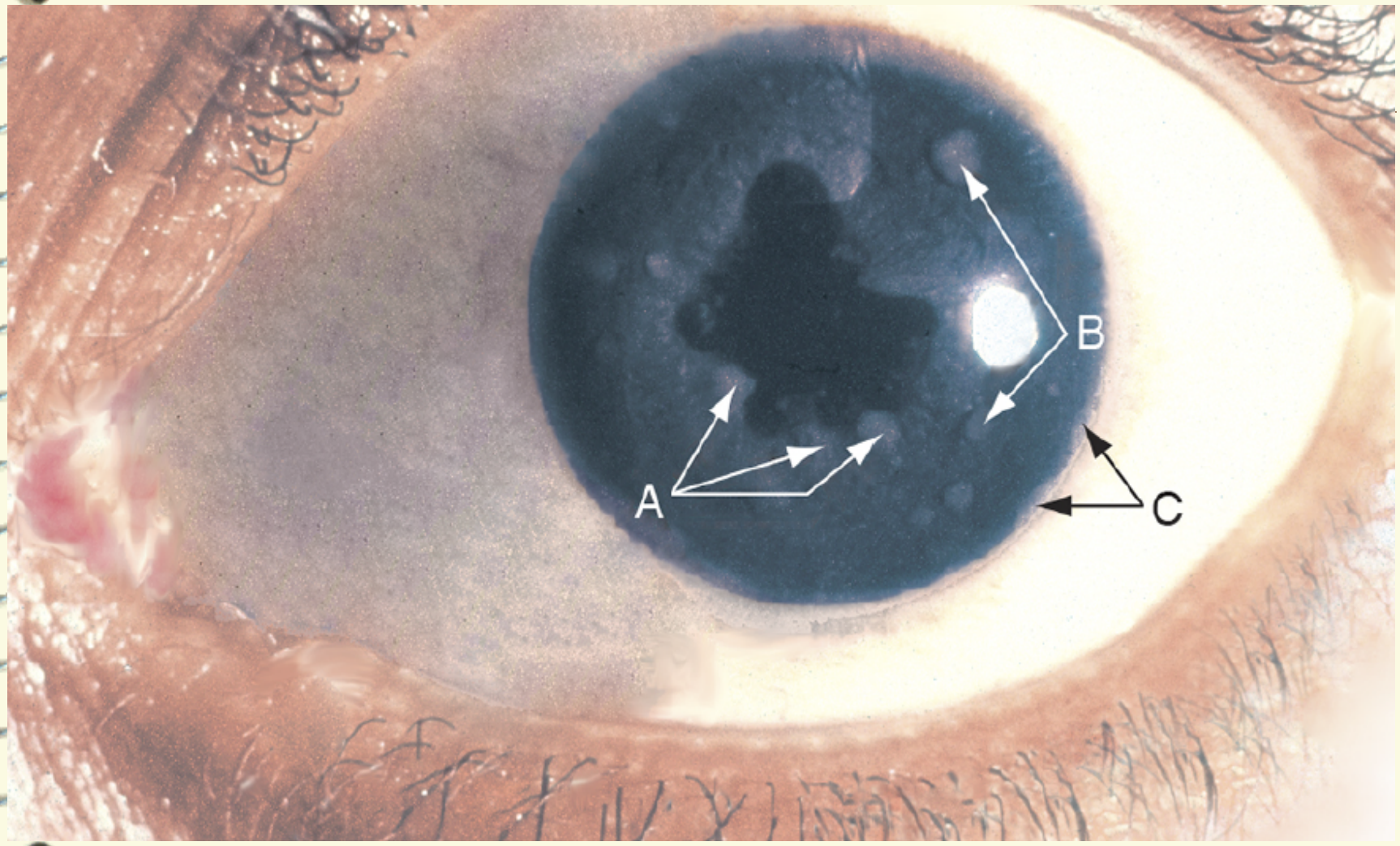








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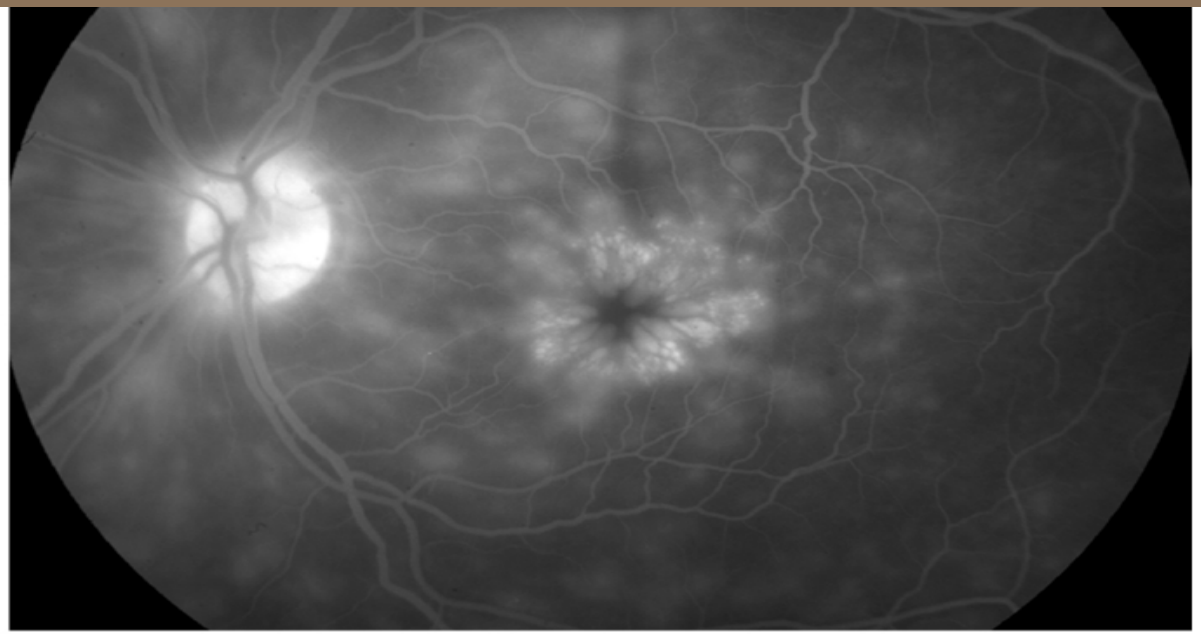


Figure 5-6 Late transit phase fluorescein angiogram of the left eye of a patient with sarcoid-associated anterior uveitis showing a petalloid pattern typical of cystoid macular edema (CME). *(Courtesy of Ramana S. Moorthy,*

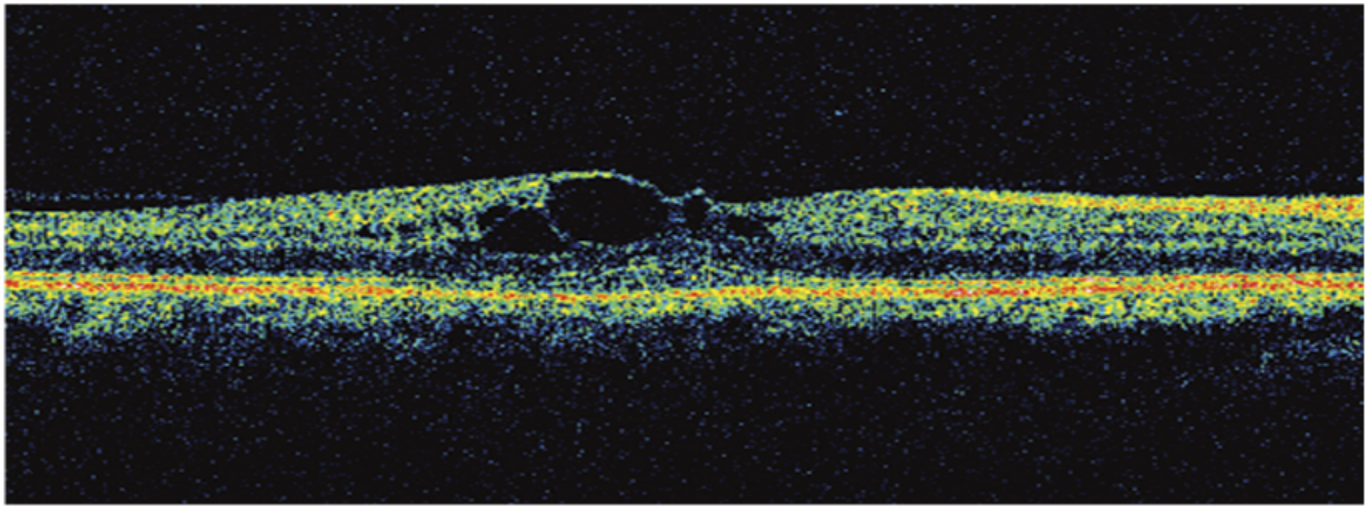


Figure 5-7 Optical coherence tomography image of the macula of the same eye as in Figure 5-6, showing cystoid spaces in the parafoveal outer plexiform layer. *(Courtesy of Ramana S. Moorthy, MD.)*

Uveitis and Systemic Disease

Table- Aetiology of Anterior uveitis

HLA-B27 Positive or Seronegative Group
Ankylosing spondylitis
Reiter's syndrome
Inflammatory bowel disease (Ulcerative colitis, Crohn's disease)
Psoriatic arthritis

Intraocular lens related
Herpes simplex
Herpes zoster
Trauma
Juvenile rheumatoid arthritis
Fuchs' Heterochromic iridocyclitis
Behcet's disease
Sarcoidosis
Tuberculosis
Syphilis
Glaucomatocyclitic crisis
Lens-induced uveitis
Idiopathic

Intermediate uveitis
Pars planitis

Aetiology of Posterior uveitis

Infection	Toxoplasma
	Histoplasmosis
	Cytomegalovirus
	Toxocara
	Herpes simplex
	Syphilis
	Tuberculosis
	Candida

Retinal vasculitis
Sarcoidosis
Sympathetic ophthalmia
Behcet's disease
Idiopathic

Heterochromia in Fuchs heterochromic iridocyclitis.

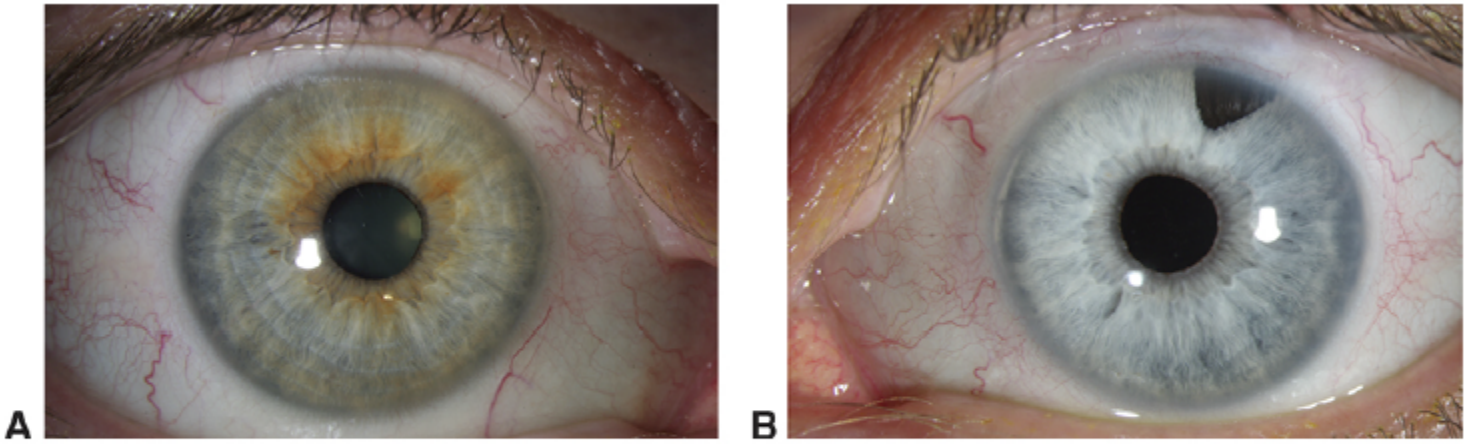


Figure 6-13 Heterochromia in Fuchs heterochromic uveitis. **A**, Right (unaffected) eye. **B**, Left (affected) eye in the same patient. Note the lighter iris color and stromal atrophy ("moth-eaten appearance") in the affected eye, which underwent surgical iridectomy at the same time as cataract surgery. *(Courtesy of H. Nida Sen, MD.)*

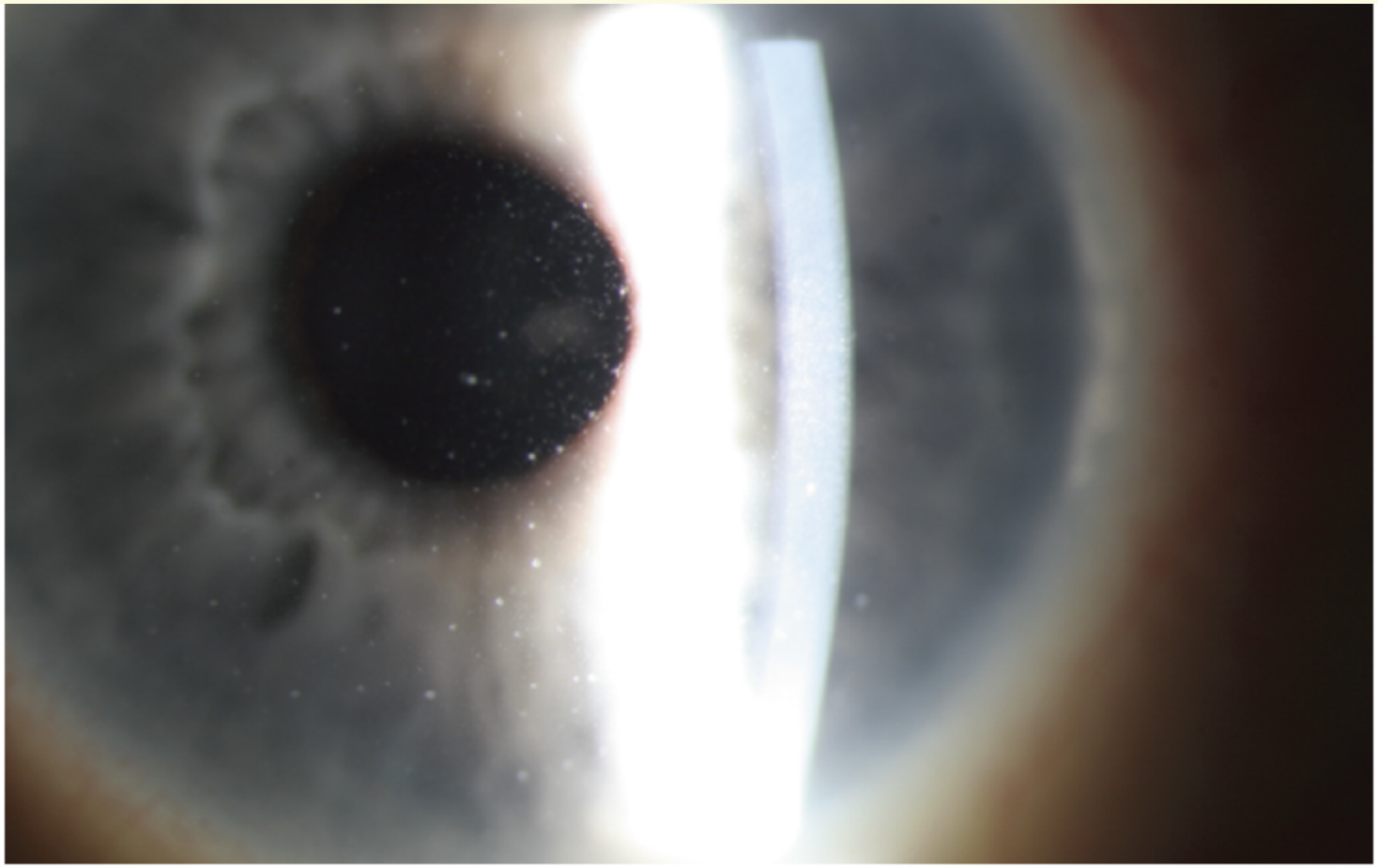


Figure 6-14 Diffusely distributed stellate keratic precipitates in a patient with Fuchs heterochromic uveitis. *(Courtesy of H. Nida Sen, MD.)*

Uveitis and Systemic Disease

HLA-B27 Antigen

The test can be useful in cases of recurrent anterior uveitis. HLA-B27 denotes a genotype located on chromosome 6. It is present in 4% of the general population and up to 50% of patients with acute iritis. Many patients with acute iritis therefore have a genetic predisposition. Factors which may trigger the occurrence of acute iritis are often unknown. In general, the importance of tissue tying for HLA B27 is under appreciated, the investigation has a high yield, is inexpensive, and gives patients an explanation of an often recurrent problem.

Ankylosing spondylitis, Reiter's syndrome, psoriatic arthritis and inflammatory bowel disease are all associated with iritis, spondylitis and the presence of HLA-B27 positivity

HLA-B27 disease.

- HLA-B27-associated AAU often presents with a number of clinical clues which help in diagnosis: it is usually recurrent, unilateral but alternating, with severe anterior chamber inflammation (posterior synechiae, fibrin and hypopyon).

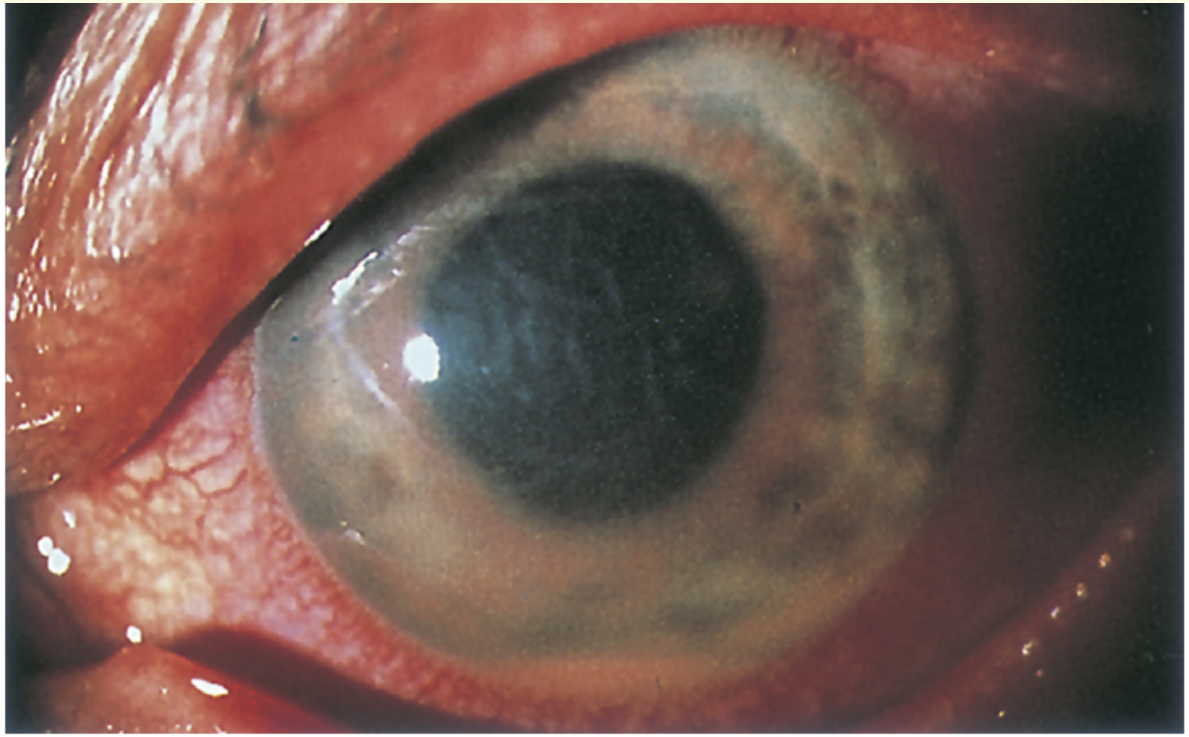


Figure 6-1 Acute HLA-B27–positive anterior uveitis that was accompanied by pain, photophobia, marked injection, fixed pupil, loss of iris detail from corneal edema, and hypopyon. *(Courtesy of David Meisler, MD.)*

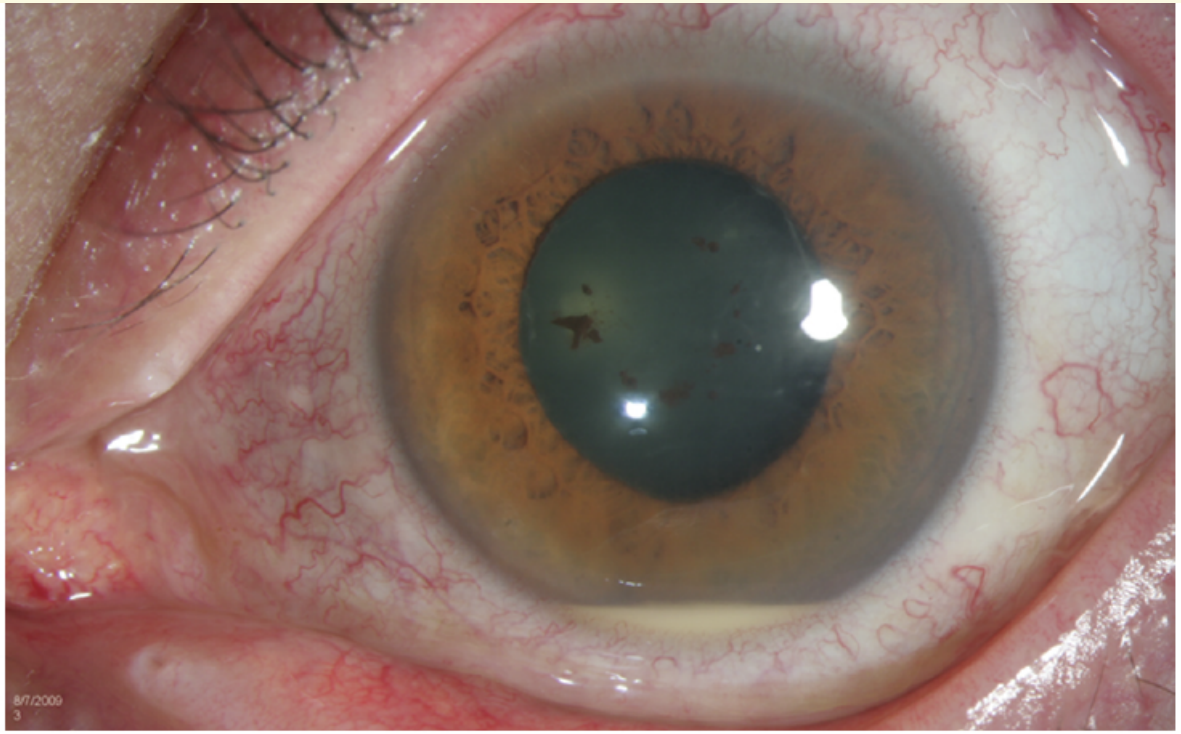


Figure 6-3 Acute nongranulomatous anterior uveitis: hypopyon and anterior capsular ring of pigment following posterior synechiolysis after intensive treatment with dilating agents. *(Courtesy of H. Nida Sen, MD.)*

Uveitis and Systemic Disease

Ankylosing Spondylitis

30% of AS patients develop iritis, especially if male; iritis may precede arthritis rarely retinal vasculitis / vitritis.
Acute anterior uveitis lasting 2-6 weeks, good prognosis.

Investigations in suspected ankylosing spondylitis
X-ray sacroiliac joints
HLA B27 (positive in more than 90%)

Reiter's Syndrome

- Occurs if genetically predisposed (HLA B27); *60 - 90% association*
- M>F
- *Exposure to certain urethritis / dysentery organisms: e.g.*
- *Chlamydia, Yersinia, Shigella, Salmonella, Campylobacter.*
- The order of manifestation is normally: Œ urethritis conjunctivitis arthritis.
- Ocular
- 20% anterior uveitis,
- 60% conjunctivitis,
- episcleritis, keratitis, post-uveitis.
- Reiter’s disease can sometimes result in hypopyon formation

Toxoplasmosis

ELISA
IgM in neonates,
Rising IgG in adults (although not that helpful in adults).
Fluorescein angiography (hypofluorescence in the early stages and then progressive leakage).
Indocyanine angiography - multiple small dark spots may be seen around the visible lesions implying the affected retina is greater than apparent initially. This sign may be useful in assessing the effect of treatment.

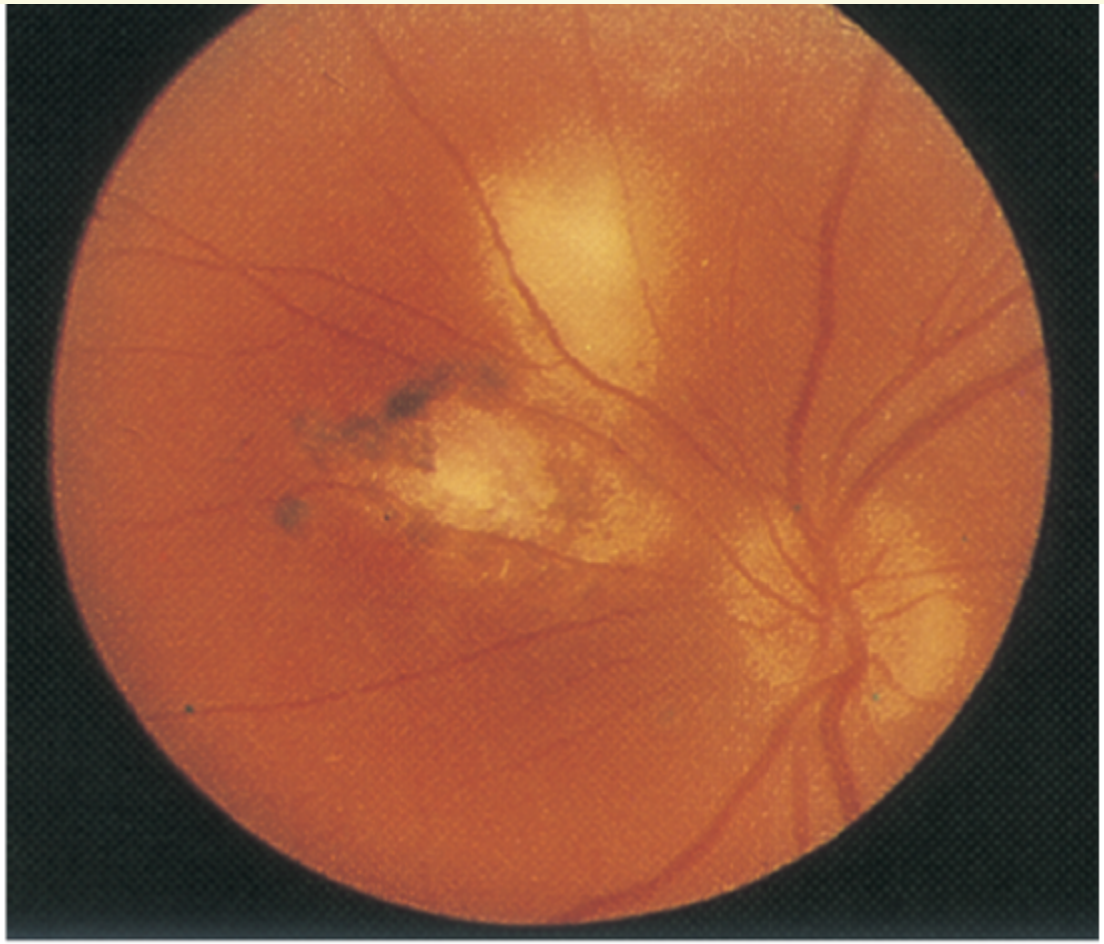


Figure 7-25 Toxoplasmosis: fundus photograph showing satellite retinochoroiditis around an old scar.

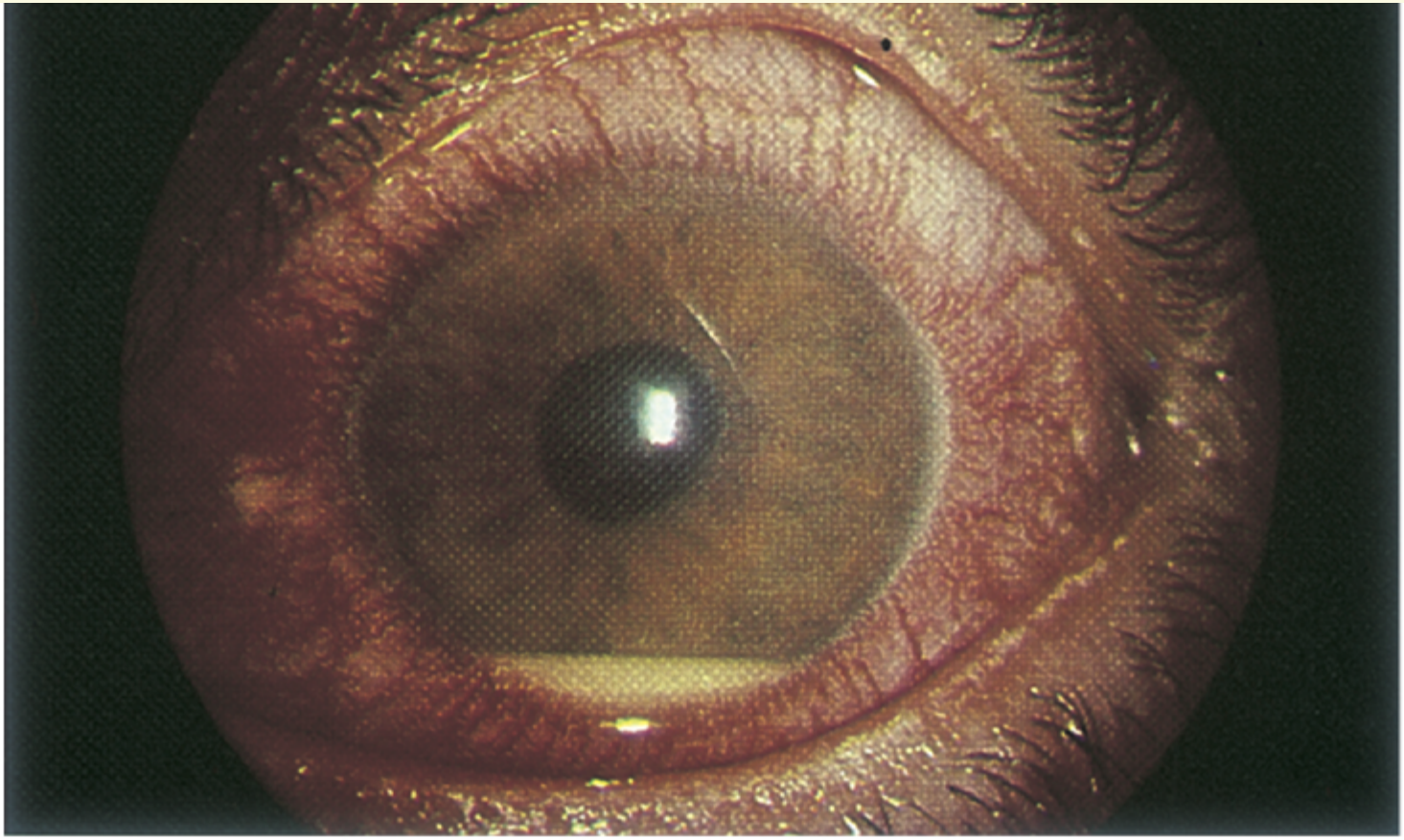


Figure 6-72 Behçet disease: hypopyon.

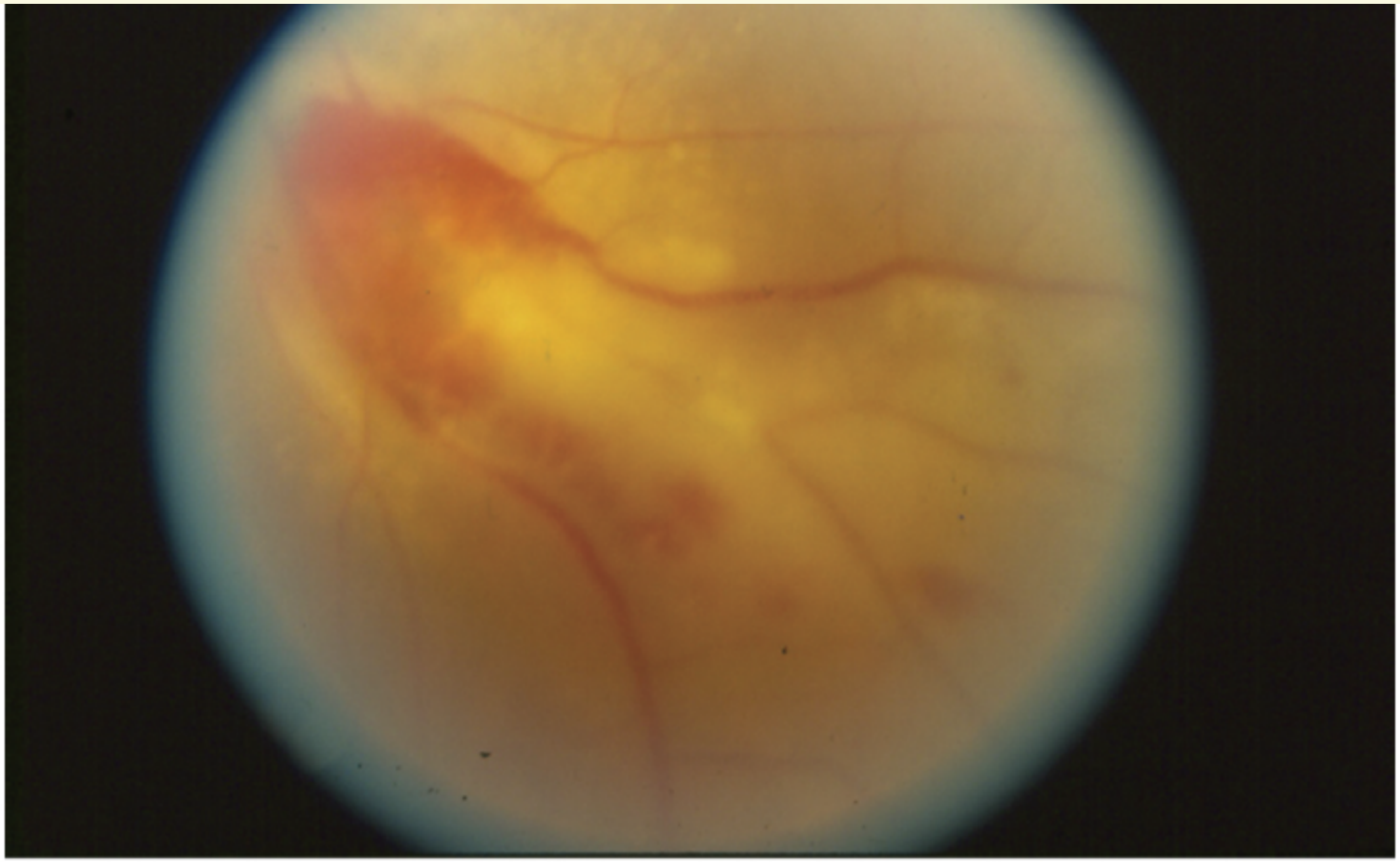


Figure 6-74 Behçet disease: fundus photograph of retinitis and vasculitis with retinal hemorrhage. The retinitis shown here appears similar to necrotizing herpetic retinitis with retinal whitening and occlusive retinal vasculitis. *(Courtesy of Ramana S. Moorthy, MD.)*

Table 6-7 Diagnostic System for Behçet Disease (Japan)

Major Criteria

- Recurrent oral aphthous ulcers
- Skin lesions (erythema nodosum, acneiform pustules, folliculitis)
- Recurrent genital ulcers
- Ocular inflammatory disease

Minor Criteria

- Arthritis
- Gastrointestinal ulceration
- Epididymitis
- Systemic vasculitis or associated complications
- Neuropsychiatric symptoms

Types of Behçet Disease

- Complete (4 major criteria)
- Incomplete (3 major criteria or ocular involvement with 1 other major criterion)
- Suspect (2 major criteria with no ocular involvement)
- Possible (1 major criterion)

Table 6-8 Diagnostic System for Behçet Disease (International Study Group for Behçet Disease)

Recurrent oral aphthous ulcers (at least 3 or more times per year) plus 2 of the following criteria:

1. Recurrent genital ulcers
2. Ocular inflammation
3. Skin lesions
4. Positive cutaneous pathergy test

Sarcoidosis

This chronic non-caseating granulomatous systemic disease of unknown
aetiology affects women more commonly than men and is more common
in individuals of Afro-Caribbean ethnicity. In Britain sarcoidosis is the commonest
systemic disease that presents as chronic uveitis.
It has protean ocular manifestations and may present with
a spectrum of ocular signs, including anterior and posterior uveitis,
retinal vascular sheathing, and optic disc abnormalities

Ocular Manifestations

About 30% of patients with sarcoidosis have ocular involvement.
Iritis may be acute or chronic; it may be unilateral or bilateral. Patients with
posterior uveitis usually have anterior uveitis as well. Vitritis is also common
and tends to occur in older patients.

There may be retinal periphlebitis; the vessels may display an exudative cuff
(so called 'candle wax drippings'). Inflammation of the retina may lead to macular
oedema, retinal granuloma, preretinal nodules and retinal

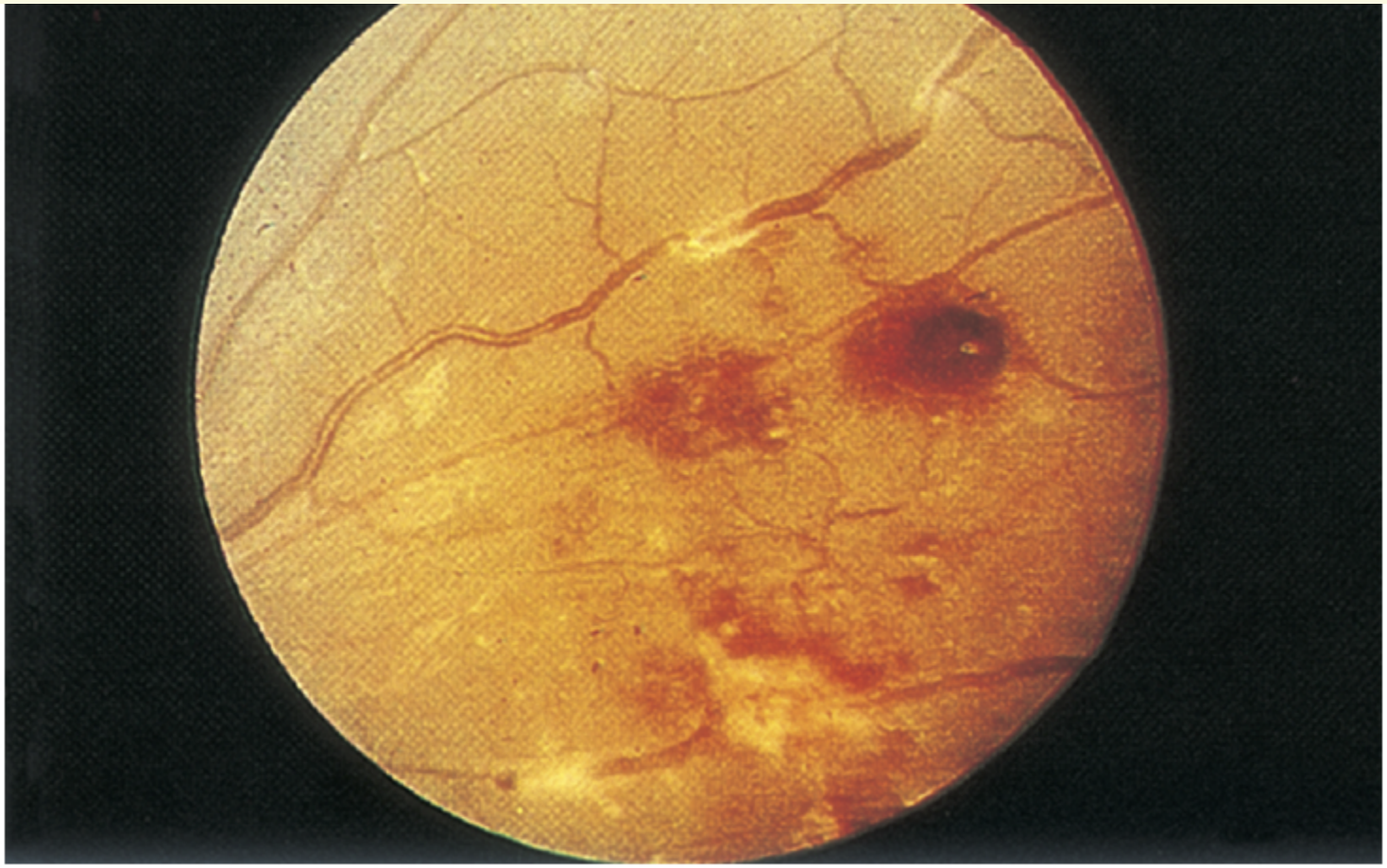


Figure 6-57 Sarcoidosis: fundus photograph showing retinal vascular sheathing.

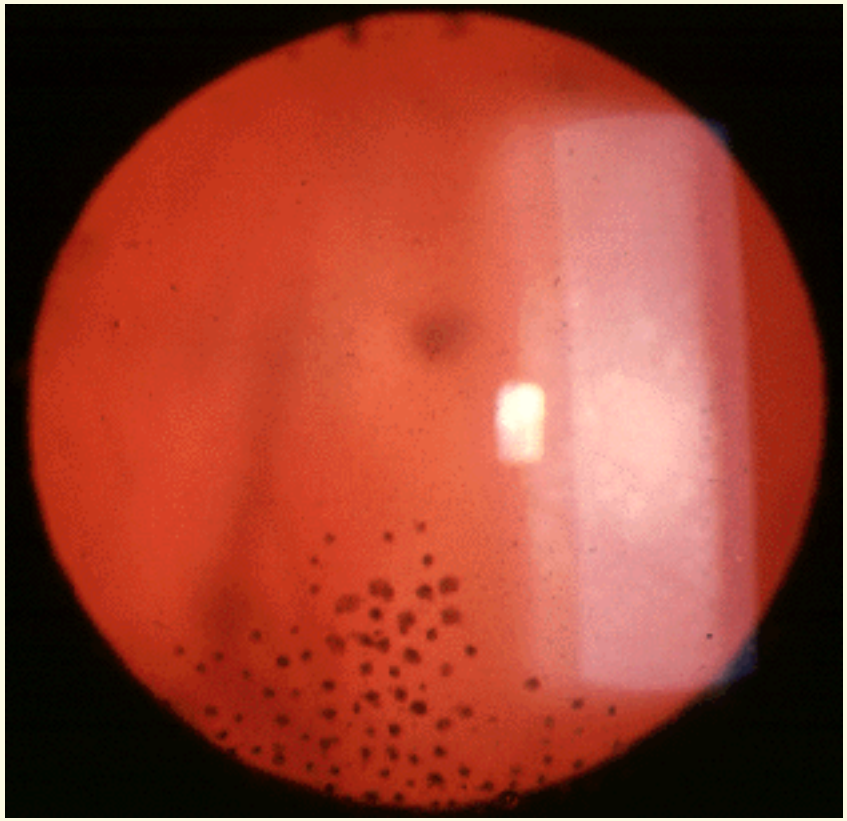
Sarciodosis - Investigations

Chest X-ray

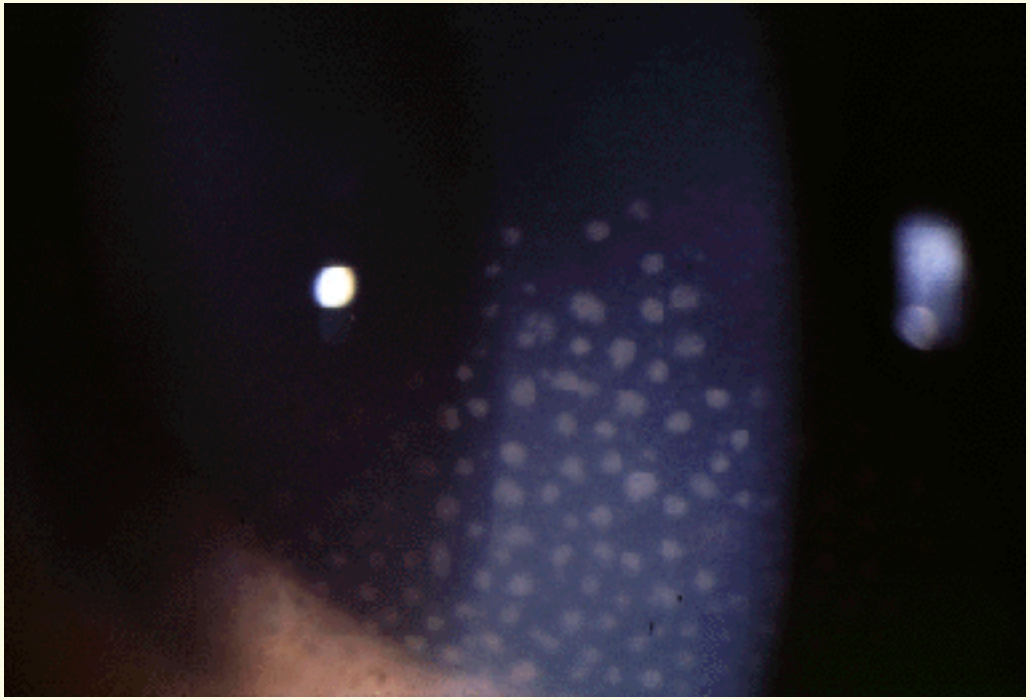
Serum ACE (angiotensin converting enzyme)- this is elevated in active disease
urine and serum calcium levels- hypercalciuria is common
hypercalcaemia is less common

Conjunctival biopsy may show granulomata

Uveitis and Systemic Disease



Uveitis and Systemic Disease



Ocular Manifestations of Tuberculosis

Affects 2% of sufferers of active tuberculosis , uveitis is commonest manifestation.
Systemic disease is often apparent.

Eyelids- lupus vulgaris (nodules surrounded by erythema)
Orbit- cellulitis, dacryoadenitis, dacryocystitis, osteomyelitis, abscess
Conjunctiva- rarely affected, chronic conjunctivitis
Cornea- phlyctenular keratoconjunctivitis, interstitial keratitis
(unilateral, sectorial, superficial vascularisation)
Sclera- episcleritis, nodular scleritis
Uveitis- chronic granulomatous anterior uveitis,
multifocal choroiditis, exudative retinitis, vasculitis, optic nerve oedema, papilloedema

Juvenile Chronic Arthritis

Chronic AAU , usually bilateral
Commoner in female patients, the young, ANF positive. Pauciarticular disease <5 joints.

Complications
Glaucoma (20%)
Cataract (40%)
Band Keratopathy (40%)

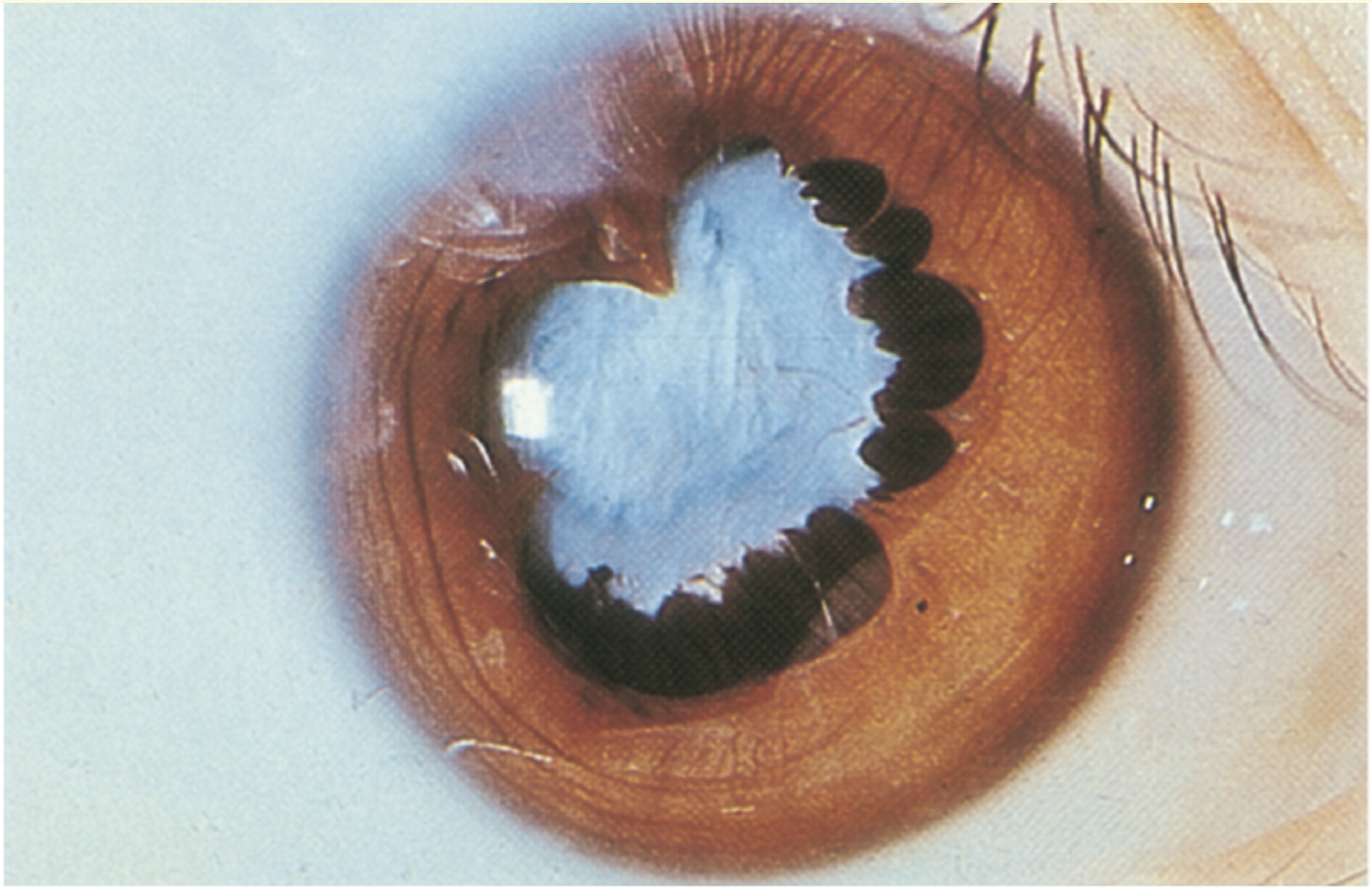
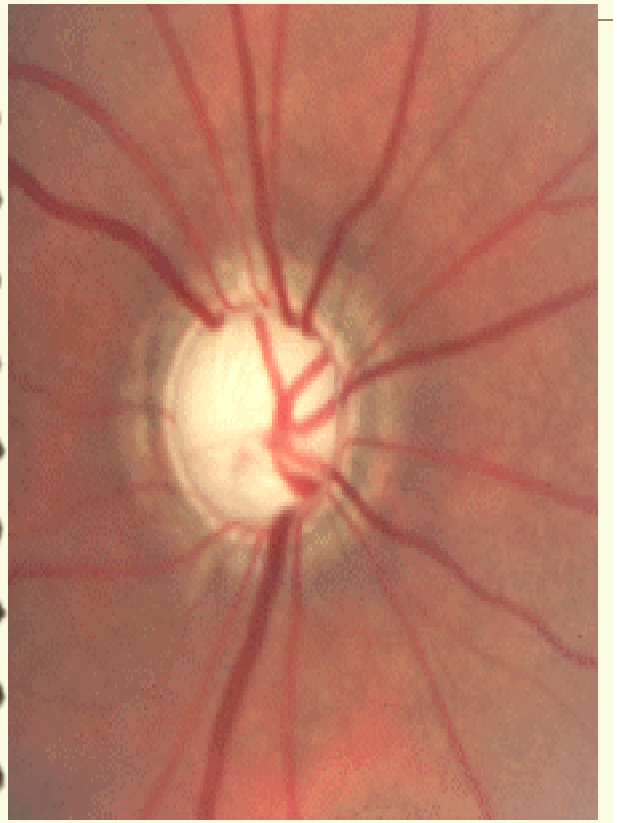


Figure 6-11 Juvenile idiopathic arthritis with chronic anterior uveitis and cataract.



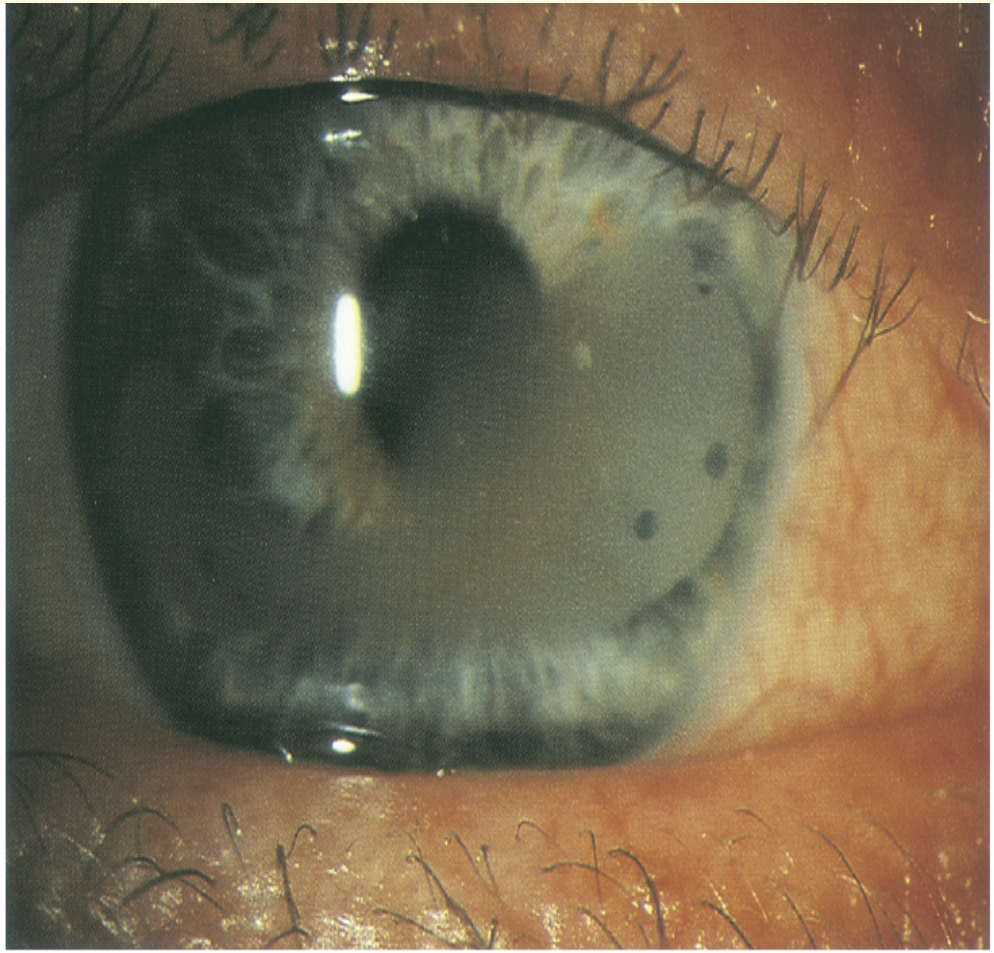


Figure 6-12 Juvenile idiopathic arthritis with chronic calcific band keratopathy.

Monitoring Children with Juvenile Chronic Arthritis

High Risk

Early Onset , < 6 years, Pauciarticular Disease , ANA Positive

3 months for first year , then 6 months for five years , then annually

Medium Risk

polyarticular disease ANA positive , pauciarticular -disease ANA negative

6 monthly intervals for 5 years then annually

Low Risk

Systemic JCA , B27 associated arthritis , disease starting after age 11

Duration

For ten years after onset of JCA or until age 12, whichever is shorter.

Source RCOphth (UK), British Paediatric Association (1994)

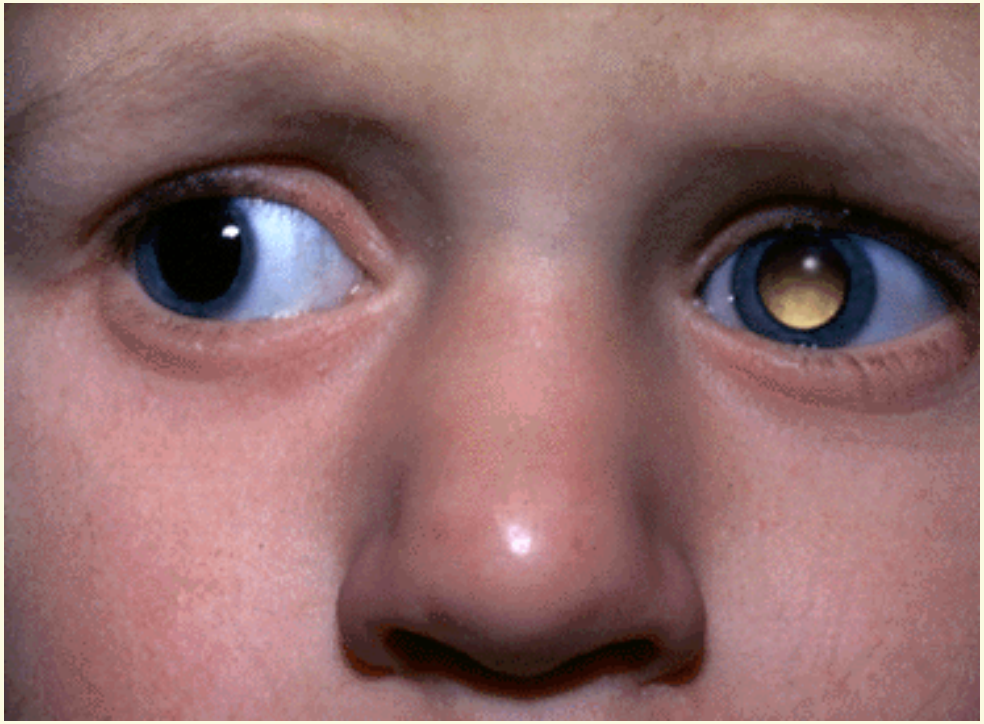
Masquerade Syndromes

Intraocular lymphoma may present as a chronic uveitis in older patients, especially when there
is vitritis and vitreous veils and a poor response to treatment. Intraocular tumours, particularly retinoblastoma in children, may also occasionally present in this manner.

Differential Diagnosis Of Uveitis- It is of paramount importance to note that uveitis can be caused or mimicked by the following-

"Masquerade Syndromes"- neoplasms mimicking uveitis
Ocular malignant melanoma
Retinoblastoma
Reticulum Cell Sarcoma (Primary Intraocular Lymphoma)
Leukaemia
Lymphoma
Ocular Metastasis

Other-
Endophthalmitis
Retinal detachment
Intraocular foreign body



Syphilis

Uveitis may be acute or chronic, unilateral or bilateral. Interstitial keratitis affects a small
percentage of acquired cases and is often unilateral.

Chorioretinitis is bilateral in 50% of cases;multifocal or diffuse yellow exudate is seen.

The chorioretinitis may resolve, leaving extensive bone spicule pigmentation.
The appearance may resemble retinitis pigmentosa.
There may be retinal oedema, haemorrhages, exudates, cotton wool spots and vascular sheathing. Optic disc oedema may also be seen.

Investigations for suspected syphilitic uveitis include VDRL and FTA-ABS tests.
The VDRL test is useful for screening; false positive results may occur.
The FTA-ABS test remains positive for life, even after treatment.

Uveitis and Systemic Disease
-History and examination

Overview of the Investigation and Management of Uveitis

The management of the patient with uveitis involves the following,

History taking (ocular and general)
Complete ocular examination
General physical examination
Investigations
Specialist medical referral (for further evaluation)

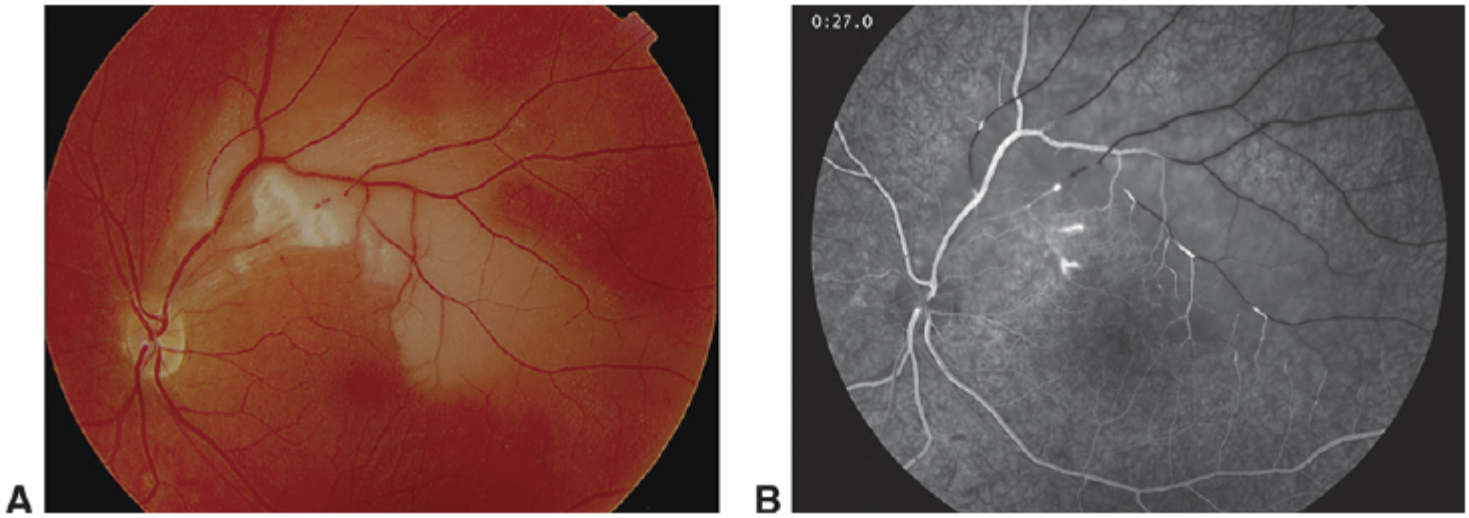


Figure 6-21 Susac syndrome. **A**, Color fundus photograph revealing an area of intraretinal whitening corresponding to a supratemporal branch artery occlusion in the left eye. **B**, Fluorescein angiogram showing a supratemporal branch artery occlusion with multiple areas of segmental staining well away from sites of bifurcation. *(Courtesy of Albert T. Vitale, MD.)*

Susac Syndrome

Susac syndrome (also known as *SICRET syndrome,* for small *i*nfarctions of *c*ochlear, *r*etinal, and *e*ncephalic *t*issue) is a rare entity, initially reported in 1979 by Susac and colleagues; it consists of the clinically observed triad of encephalopathy, hearing loss, and retinal artery branch occlusions. The syndrome occurs mostly in young women but has been noted in patients aged 16–58 years. Differential diagnosis at presentation includes MS, herpetic encephalitis, acute disseminated encephalomyelitis, and Behçet disease. However, ocular findings are highly specific and allow prompt diagnostic confirmation with subsequent therapeutic adjustments. Ophthalmoscopy shows diffuse or localized narrowing of retinal arteries with a "boxcar" segmentation of the blood column at the level of peripheral retinal arteries. Vitreous haze or cells are absent. Retinal FA discloses focal nonperfused retinal arterioles with hyperfluorescent walls (Fig 6-21). There is usually no evidence of embolic material or inflammatory reactions around the vessels. Magnetic resonance imaging (MRI) is another useful diagnostic tool and shows multifocal supratentorial white matter lesions; the corpus callosum may be involved. Audiometry should be performed in any patient being evaluated for this entity; sensorineural hearing loss is a common finding. Treatment remains controversial and includes high-dose intravenous corticosteroids, anticoagulants, and IMT. The course of Susac syndrome is not always self-limiting, and isolated retinal arteriolar involvement may occur as a very late manifestation.

When to investigate

- One of the most pressing questions that arises in the mind of every ophthalmologist who sees a new case of uveitis is "what is the cause of this disease?" In evaluating patients with uveitis, the ophthalmologist must consider that a lengthy list of infections, autoimmune systemic diseases, distinctive inflammatory conditions and masquerade syndromes may all cause uveal inflammation. Despite this array of potential diagnoses, the vast majority of patients have disease that defies

General Investigations

- A recent retrospective review of patients with various types of uveitis showed the following abnormal results: full blood count: 23/113 (20.3%), plasma viscosity / ESR: 37/108 (34.2%), VDRL/TPHA: 3/70 (4.3%), angiotensin converting enzyme (ACE): 9/77 (10.8%) and chest x-ray (CXR): 15/103 (14.6%). Sarcoidosis was diagnosed in eight patients who had an abnormal CXR ± raised ACE.
- All patients with symptoms of other organ system dysfunction or general malaise should be investigated to rule out under-lying systemic disease.

Uveitis and Systemic Disease

Table Uveitis - Investigations

General Investigations

ESR / Plasma Viscosity/ C Reactive Protein
CXR
FBC
Syphilis Serology- TPHA, VDRL
Urine analysis (Diabetes Mellitus)

Specific Investigations

HLA B27 Ag; HLA B29 (birdshot retinochoroidopathy)
Angiotensin Converting Enzyme
Rheumatoid Factor , Lupus Group Autoantibodies including anti-neutrophil cytopasmic antibody (Wegener's Granulomatosis) Anticardiolipin Antibody- (the yield of these investigations is actually low except in children with Juvenile Chronic Arthritis)
Toxoplasma Serology / IgG antibodies (if negative on undiluted serum to exclude congenital toxoplasmosis)
Toxocara ELISA
HIV
Pathergy Test
Mantoux Test, Sputum Acid Fast Bacilli
X Ray Hands and SI Joints
B Scan for Masquerade Leisions or Posterior Scleritis
Kveim Test
Immune Complexes -Polyethylene Glycol Method
DNA Polymerase Chain Reaction (Herpes virus, Propionebacter)
CT scan of chest (sarcoidosis)
MRI(non Hodgkins lymphoma, neurosarcoid, demyelination)
Choroidal biopsy (Non Hodgkin's Lymphoma)

Physician Referral

Rheumatological Referral
Broncho-alveolar lavage (Sarcoid)
CSF studies (non Hodgkins lymphoma, neurosarcoid, VKH)
Venereological Referral HIV, Reiter's, Syphilis

A recent retrospective review showed the following abnormal results, plasma viscosity/ esr 34.2%, VDRL/TPHA (4.3%) Angiotensin converting enzyme (10.8%) Chest X ray (14.6%)

Useful investigations for chronic uveitis

- *Chest x ray* Diagnosis of tuberculosis, sarcoidosis, lymphoma, lung carcinoma
- *Syphilis serology* Diagnosis of syphilis
- *HLA-A29* Diagnosis of birdshot chorioretinopathy
- *Mantoux test* Anergic response despite prior BCG vaccination is consistent with sarcoidosis. Strong positive response without prior vaccination suggests exposure to tuberculosis
- *HIV serology* If patient of high risk status or clinical picture suggests HIV related uveitis such as cytomegalovirus retinitis
- *Lyme disease serology* If patient from endemic area or with history of exposure and suggestive symptoms
- *Antinuclear antibodies* If clinical picture suggests juvenile chronic arthritis ANF ANCA Rhem Factor
- *Aqueous and vitreous biopsies* Diagnosis of infective endophthalmitis and intraocular lymphoma

Therapeutics

- The aims of treatment are to control inflammation, prevent visual loss, and minimise long term complications of the disease and its treatment. Macular oedema is the commonest indication for treatment. Treatment is usually indicated if the visual acuity has fallen to less than 6/12, or if the patient is experiencing visual difficulties. In patients with longstanding macular oedema and poor vision or where it is not possible to determine easily the cause of visual loss, a trial of immunosuppressive treatment is usually indicated to determine whether the visual loss is reversible. Many patients with unilateral chronic uveitis can be managed with topical corticosteroids to control anterior uveitis and periocular corticosteroids for macular oedema and visual loss. Patients with useful vision in only one eye must be managed aggressively to control inflammation and preserve vision.

Systemic corticosteroids

- Corticosteroids are the mainstay of systemic treatment for patients with chronic uveitis, and the usual indication for treatment is the presence of macular oedema and visual acuity of less than 6/12.
- Patients should be treated with appropriate doses to determine whether the macular oedema is reversible. Thus maximum treatment (1.0-1.5 mg/kg body weight/day of prednisone or prednisolone) should be used for two to three weeks.
- If there is no response at this dose, addition of a second line agent such as cyclosporin (or azathioprine or mycophenolate in older patients) for a further four to six weeks may be

systemic immunosuppressive therapy

- If macular oedema recurs and visual acuity decreases at an unacceptably high dose of corticosteroid (>15 mg/day of prednisolone) an additional drug is necessary to help control the inflammation. Cyclosporin is the drug of choice for most patients aged under 50 years.The commonest dose limiting side effects of cyclosporin are hypertension and renal dysfunction, which are usually reversible if the drug is stopped.
- Several other drugs can be considered in patients who require additional immunosuppressive therapy when cyclosporin is not appropriate or not tolerated. Azathioprine, methotrexate, and, much less commonly, cyclophosphamide are the most used, but each is associated with important side effects and complications. Other agents such as mycophenolate, tacrolimus, and Anti TNF have been used.Treatment is likely to last for a minimum of six months and is often much longer.

Surgery

- Surgery may be required for complications such as cataract, glaucoma, and vitreoretinal problems, but, except in emergency situations, it should be contemplated only once the uveitis is controlled, ideally for at least three months. Intraocular surgery (cataract removal, vitrectomy, and retinal detachment surgery) is performed under the cover of systemic corticosteroids to prevent a relapse of uveitis. Removal of the vitreous body (vitrectomy) may be helpful when there is substantial opacity but also may improve disease control, particularly in younger patients.

Complications of chronic uveitis and their management

- **Macular oedema**
- Periocular steroids
- Systemic steroids
- Immunosuppressive drugs
- **Cataract**
- Surgery once uveitis controlled for 3 months preoperatively
- Perioperative cover with corticosteroid
- Intraocular lens in most patients
- **Glaucoma**
- Management depends on type
  Topical drugs
  Short term treatment with systemic carbonic anhydrase inhibitors
  Surgery
- **Synechiae**
- Minimise with regular mydriatics
- **Band keratopathy**
- Chelation with EDTA
- Excimer laser
- **Vitreous opacities**
- Observation
- Occasionally short course of corticosteroids
- Vitrectomy rarely required
- **Vitreous haemorrhage**
- Observation
- Exclude new vessels and retinal tear as cause
- **Retinal neovascularisation**
- Control uveitis
- Laser photocoagulation if ischaemia present
- **Subretinal neovascularisation**
- Observation
- Laser photocoagulation
- Interferon a
- Surgical membranectomy
- **Retinal detachment**
- Determine whether exudative, rhegmatogenous, or traction
- Surgery usually involves vitrectomy
- Perioperative cover with corticosteroid

Complications from chronic uveitis

Complications from chronic uveitis are common and may result in severe visual loss..

M*acular oedema* can complicate any type of uveitis and can cause substantial visual loss.

- *Cataract* is common in chronic uveitis and its treatment with corticosteroids. Techniques for cataract surgery and perioperative management have improved greatly, and most patients with uveitis are now suitable for intraocular lens implantation and do well.[18]
- *Glaucoma* is the most overlooked complication of chronic uveitis and has several causes.[19] Medical management with topical agents such as blockers control the elevation of intraocular pressure in most patients. Some patients also require oral carbonic anhydrase inhibitors, while surgical intervention is reserved for those who have progressive visual loss or uncontrollable intraocular

Summary points

- Intraocular inflammation has various causes and can be acute or chronic
- In either case the inflammatory process can be apparently localised to the eye or be part of a systemic disease such as sarcoidosis or Behçet's disease
- The inflammation can occur in any part of the eyeanterior, posterior, or bothand visual loss can occur with any type
- Treatment depends on the location and severity of the inflammation, with systemic drugs being reserved for sight threatening posterior disease
- Complications are common and include cataract, glaucoma, macular oedema all of which can