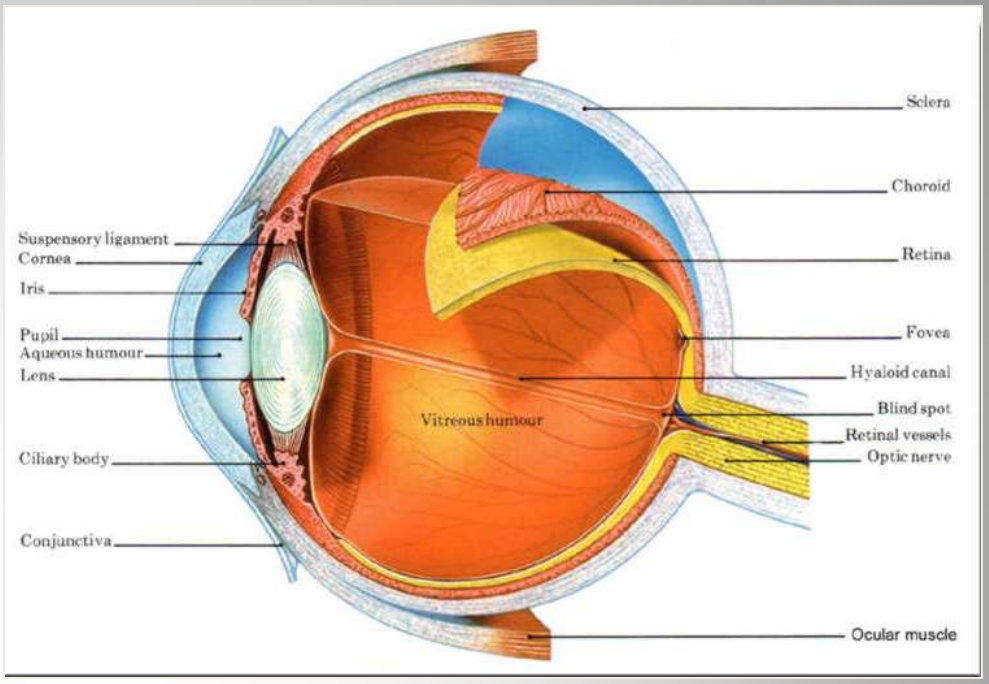
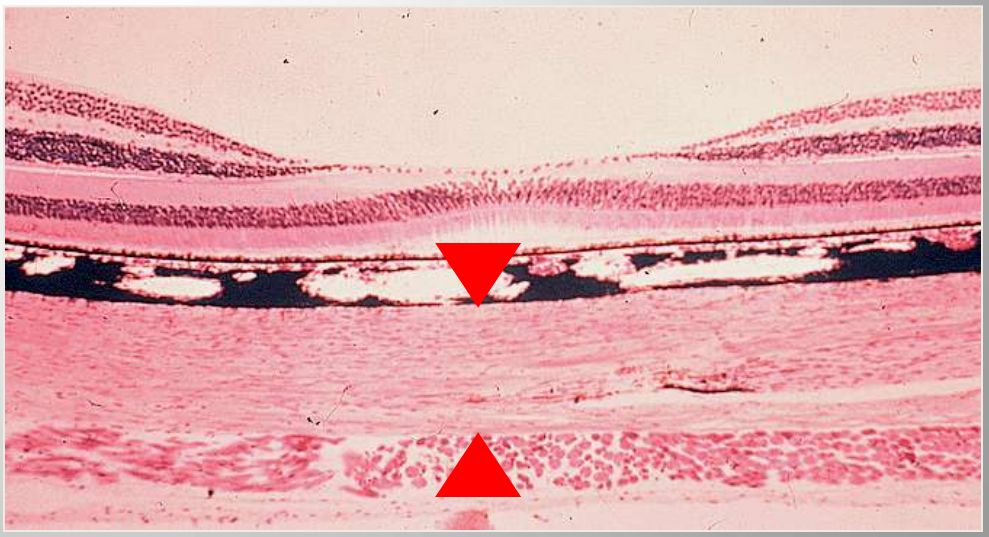
Episcleriti e scleriti

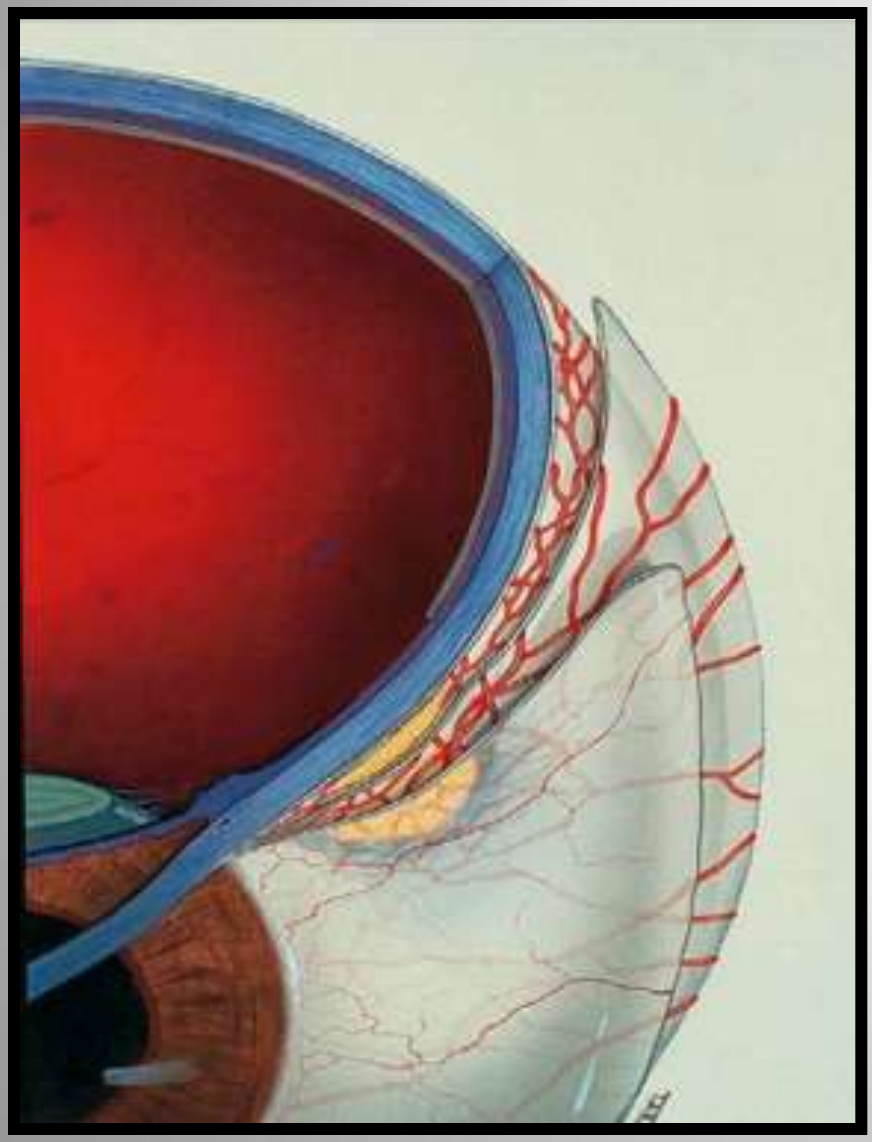
Chiara Spinelli
Clinica Oculistica
Az. Ospedaliera Universitaria Integrata
Verona

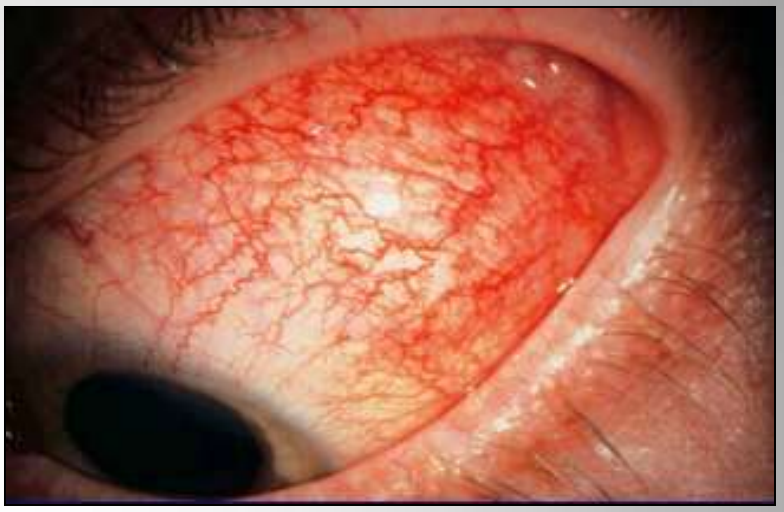
- **Anatomia**
  - Episclera
  - Sclera
  - Lamina fusca
- **Istologia**
  - collagene (70-80%)
  - proteoglicani, elastina, fibroblasti
- **Innervazione**
  - nervi ciliari posteriori (brevi-lunghi)
- **Vascolarizzazione**
  - a. ciliari posteriori lunghe
  - a. ciliari anteriori
  - 3 plessi vascolari
    - congiuntivale bulbare
    - episclerale superficiale
    - episclerale profondo

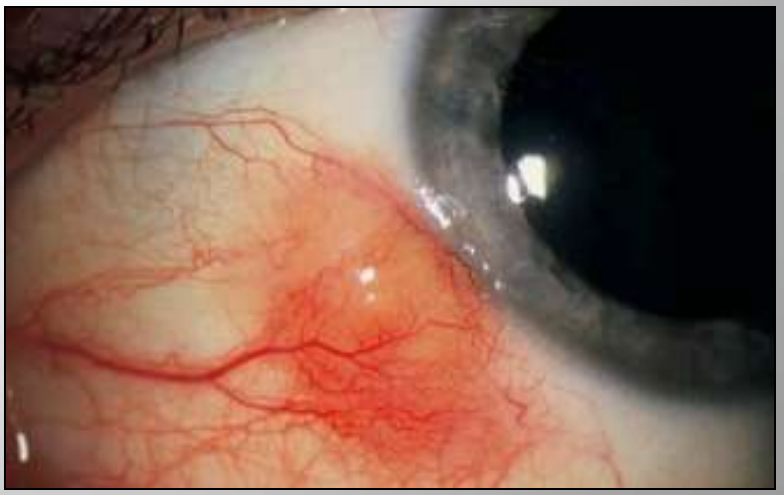




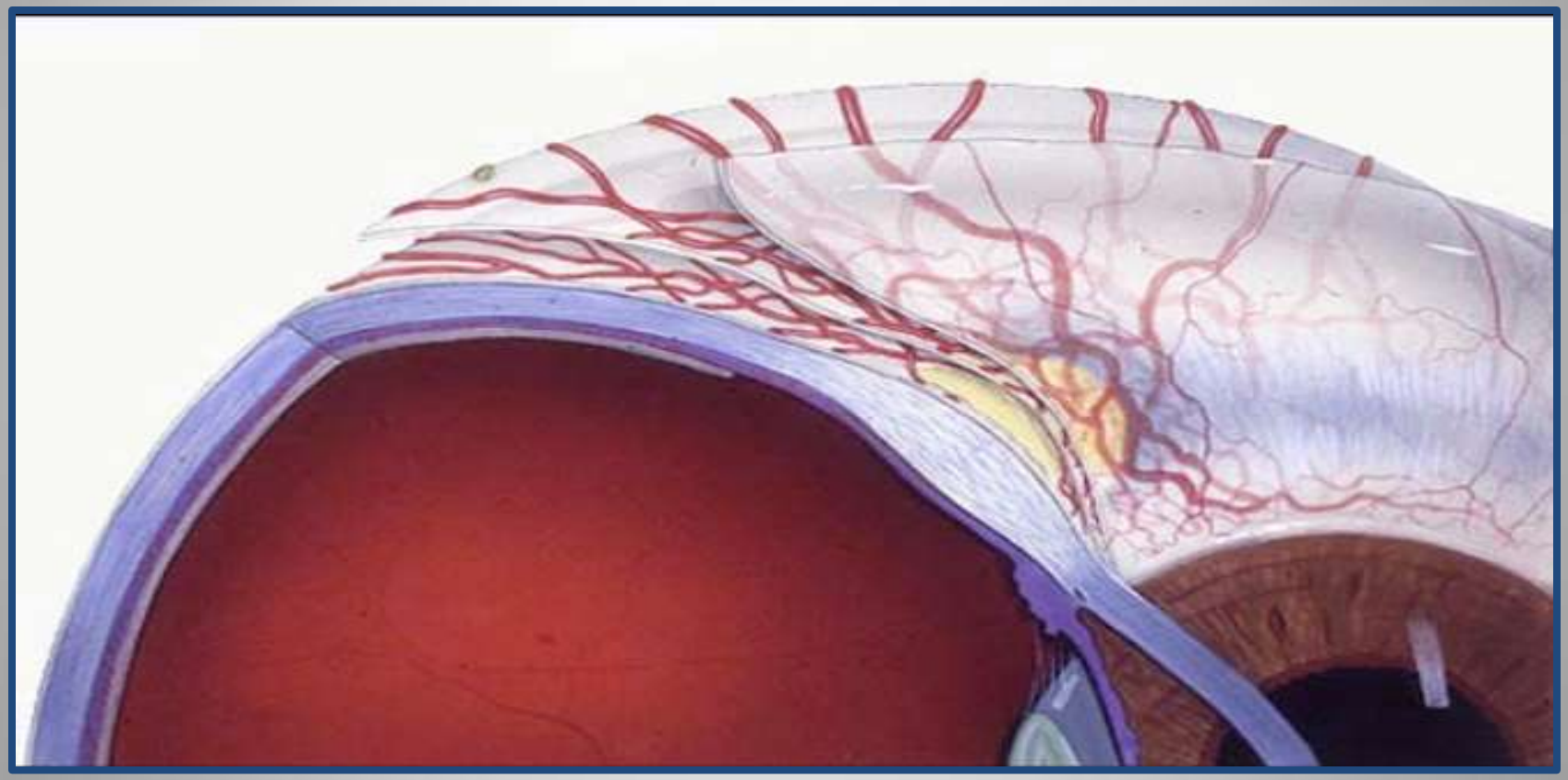
Episclerite







Sclerite



Ophthalmologic Manifestations of Rheumatic Diseases

Fayad Hamideh and Pamela E. Prete

Ocular Disorder	Rheumatic Disease
Dry eyes (sicca syndrome)	Rheumatoid arthritis[37]
	Systemic lupus erythematosus[135]
	Scleroderma[166]
	Primary Sjögren's syndrome[15]
Uveitis	
Acute anterior uveitis	Spondyloarthropathies[92]
	Behcet's disease[2]
	Inflammatory bowel disease[90]
Chronic anterior uveitis	Inflammatory bowel disease[90]
	Relapsing polychondritis[20]
Panuveitis	Behcet's disease[2]
Scleritis	Rheumatoid arthritis[42]
	Vasculitis, especially Wegener's granulomatosis[205]
	Inflammatory bowel disease[92]
	Relapsing polychondritis[20]
Keratitis	
Non-necrotizing corneal melt	Sjogren's syndrome[15]
	Rheumatoid arthritis[41]
Necrotizing keratitis	Rheumatoid arthritis[49]
	Vasculitis[255]
Retinal vasculopathy	
Microvasculopathy	Systemic lupus erythematosus[144]
Diffuse vaso-occlusive disease	Systemic lupus erythematosus[144]
	Antiphospholipid antibody syndrome[159]
	Behcet's disease[2]
Optic nerve disease	
Ischemic optic neuropathy	Vasculitis, especially giant cell arteritis[216]

Classification of Scleral Inflammation

Type	Subtypes
Episcleritis	Diffuse
	Nodular
Anterior Scleritis	Diffuse
	Nodular
	Necrotizing
	With inflammation
	Without inflammation
	Scleromalacia perforans
Posterior Scleritis	Diffuse
	Nodular
	Necrotizing (at least on histopathology)

Watson PG, Hayreh SS. Scleritis and episcleritis. Br J Ophthalmology 1976.

Ophthalmol 2000;130:469–476.

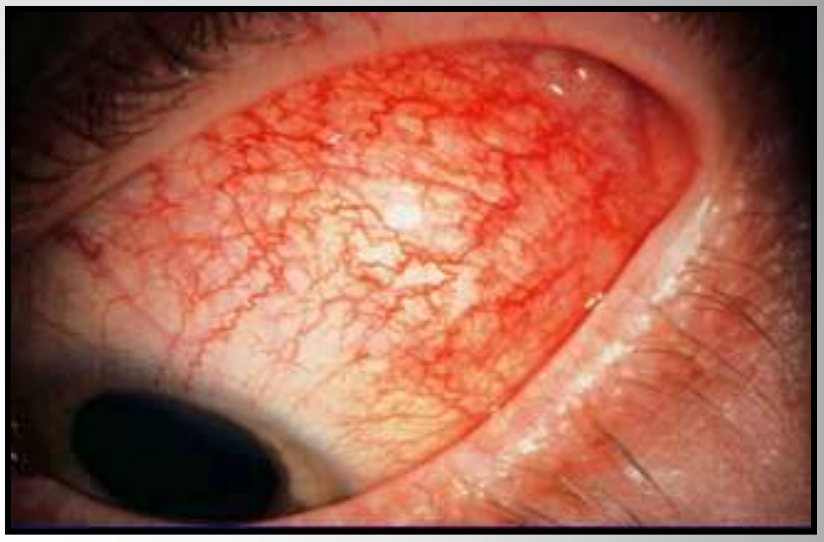
scleritis in the demographic characteristics of age, gender, and race. The occurrence of bilateral disease was similar between the two groups. Ocular complications occurred in nearly 60% of patients with scleritis but in only 13.5% of patients with episcleritis ($P < .0001$). No patient with episcleritis had a decrease in visual acuity, whereas nearly 16% of patients with scleritis did. Although there was a suggestion that associated rheumatic diseases were more common in patients with scleritis (39.2%) than in episcleritis (29.7%), the difference was not statistically significant ($P = .326$).

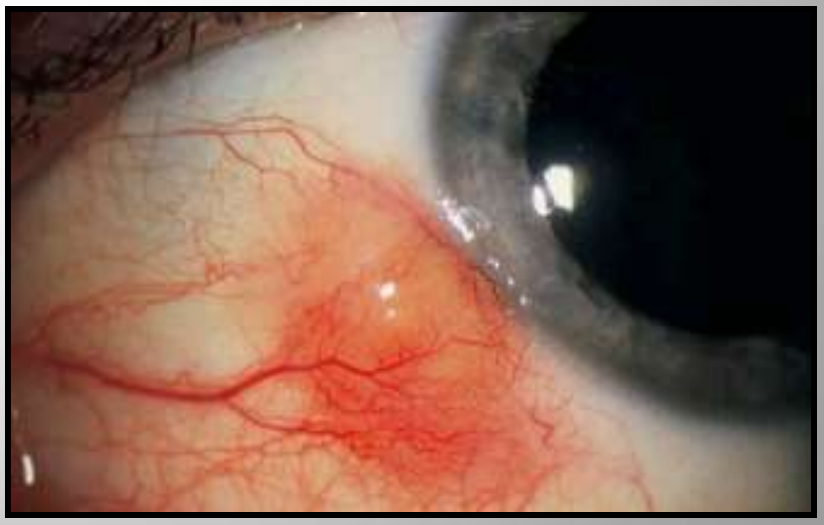
Thirty of the patients (81.1%) with episcleritis had simple episcleritis, and seven (18.9%) had nodular episcleritis. One hundred twenty-six of the patients (94%) with scleral inflammation maintained the same type of scleral inflammation throughout the course of their disease. Two patients with episcleritis at their initial presentation subsequently evolved into scleritis during the follow-up. Six patients with scleritis progressed to another subtype throughout the course of follow-up. Of the two patients with episcleritis who progressed, one had rheumatoid arthritis. Of the six patients with scleritis whose subtype changed, five had an associated systemic disease.

Of the 18 patients with episcleritis and bilateral disease, 12 presented with bilateral disease and six developed inflammation in the second eye during follow-up. The risk of second eye involvement in a patient presenting with unilateral episcleritis was 12% at 1 year. There was no significant correlation between the development of bilateral disease during follow-up and the subtype of episcleritis, the presence of systemic disease, or the maximum treatment required for control of the disease. Of the 49 patients with bilateral scleritis, 29 had bilateral disease at their initial presentation, and 20 presented with unilateral disease and subsequently developed bilateral disease. The

Episclerite

- Fisiopatologia: poco conosciuta
- Clinica:
  - arrossamento e dolore modesto
  - semplice, nodulare
  - benigna, autolimitante, ricorrente





Episcleriti

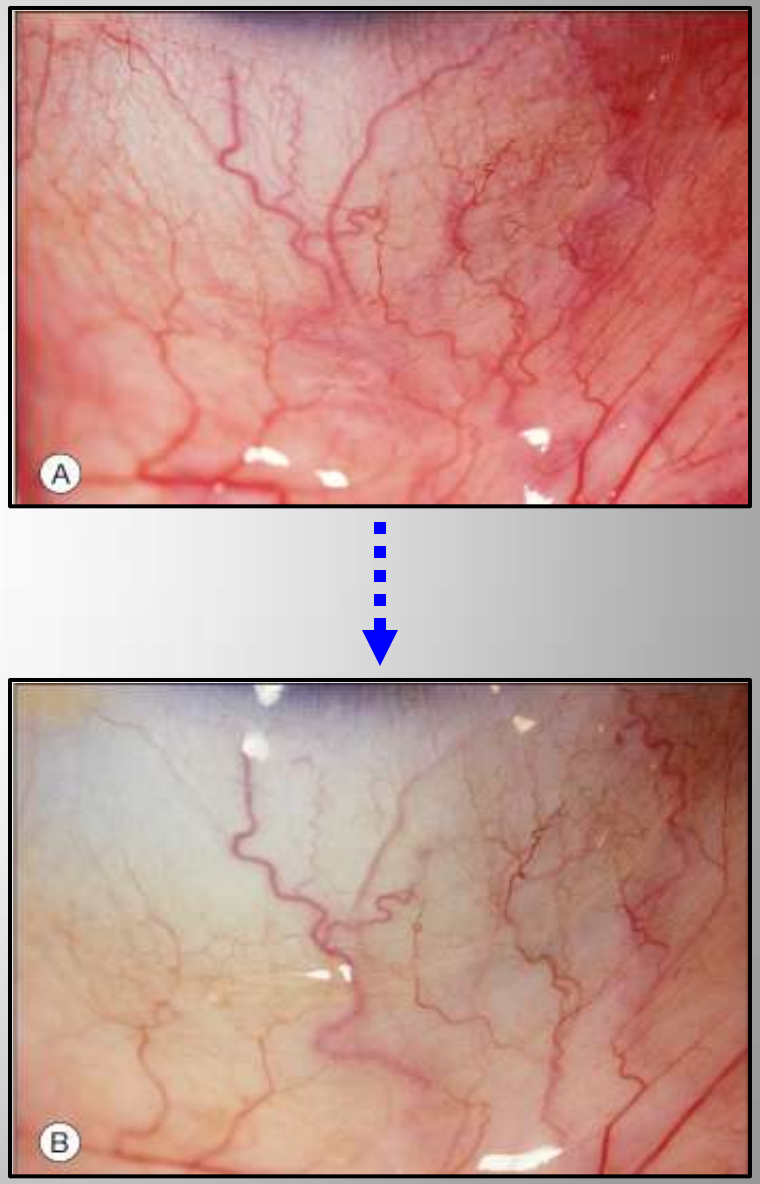
Eziologia:

- Idiopatica (2/3 casi)
- Generalmente non associata a malattie sistemiche:
  - Malattie del connettivo/vasculiti (13%)

    (AR, LES, PAN, Gr. di Wegener, spondiliti sieronegative)
  - Gotta
  - Infettive (HSV, TCB, sifilde, m. di Lyme…)
  - Miscellanea (IBD, atopia, rosacea)

Work-up:

- Storia clinica
- Test fenilefrina
- Esami ematochimici:
  - VES, PCR
  - Ac. urico
  - FR
  - ANA
  - ACE
  - VDRL test



Trattamento episclerite

- Episodio iniziale:
  - Lubrificazione
  - FANS topici inefficaci
  - Evitare steroidi topici per il loro effetto rebound/collaterale (ma utili nelle forme nodulari)
- Episclerite associata a herpes, rosacea, gotta, atopia:
  - Trattamento della malattia di base
- Episclerite ricorrente o associata a specifiche malattie del connettivo:
  - FANS sistemici

Sclerite

- Patogenesi:
  - Patogenesi poco nota (occhi enucleati/biopsie su sclere necrotiche)
  - Malattia immuno-mediata (interazione di fattori genetici e ambientali)
- Incidenza:
  - Rara (0.08-2.6%)
- Sesso:
  - F:M=1.6:1
- Non fattori razziali/geografici
- Età:
  - 4°-6°decade

Eziologia

- Isolata (43%)
- Autoimmune (48%):
  - Malattie del connettivo
  - Vasculiti
- Infettiva (7%)

  HSV, Toxo, Lue…
- Miscellanea (2%)

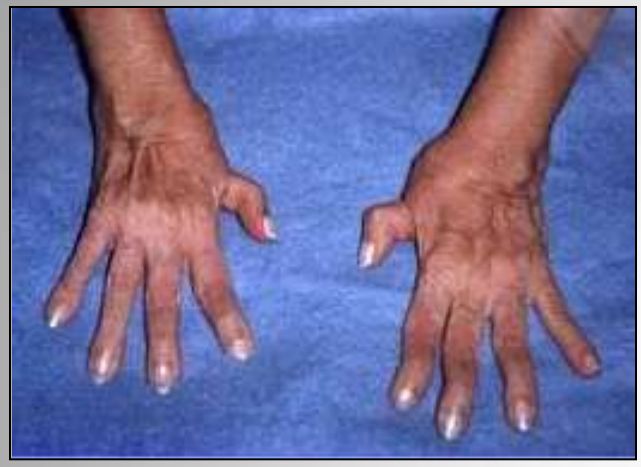
Table 1 Frequency of systemic disease among patients with scleritis.[1–3,a]

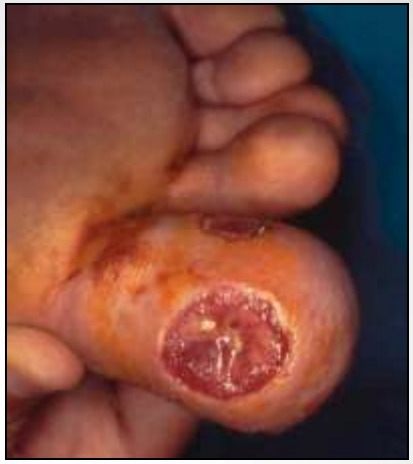
Disease	Percentage of patients
Rheumatoid arthritis	10.3–18.6
Wegener's granulomatosis	3.8–8.1
Relapsing polychondritis	1.6–6.4
Systemic lupus erythematosus	1.0–4.1
Inflammatory bowel disease	2.1–4.1
Seronegative spondyloarthropathies—ankylosing spondylitis, reactive arthritis, psoriatic arthritis	0.3–3.5
Polyarteritis nodosa	0.4–1.1

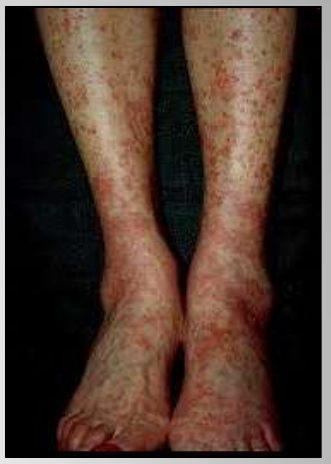
[a]Data are derived from three large series. Other systemic immune-mediated diseases that were present in patients with scleritis but affected less than 1% of the total, included Behçet's disease, Takayasu's disease, giant cell arteritis, hypersensitivity urticarial vasculitis, cutaneous vasculitis, hepatitis C-associated vasculitis, undifferentiated connective tissue disease, polymyalgia rheumatica, pyoderma gangrenosum, sarcoidosis and Cogan's syndrome.

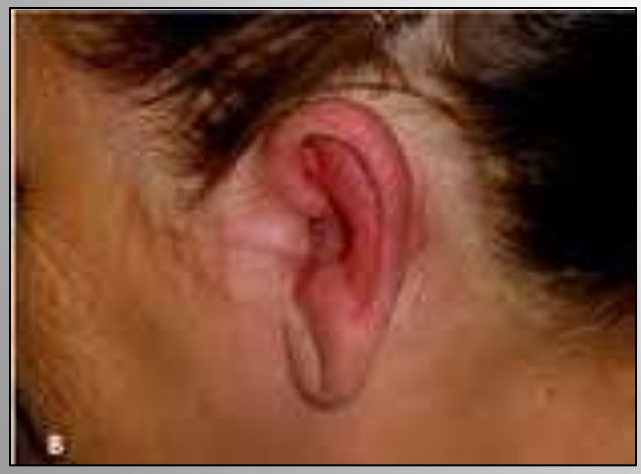
Smith J R *et al*. (2007) Therapy Insight: scleritis and its relationship to systemic autoimmune disease *Nat Clin Pract Rheumatol* **3:** 219–226.

Scleriti ⇄ malattie sistemiche







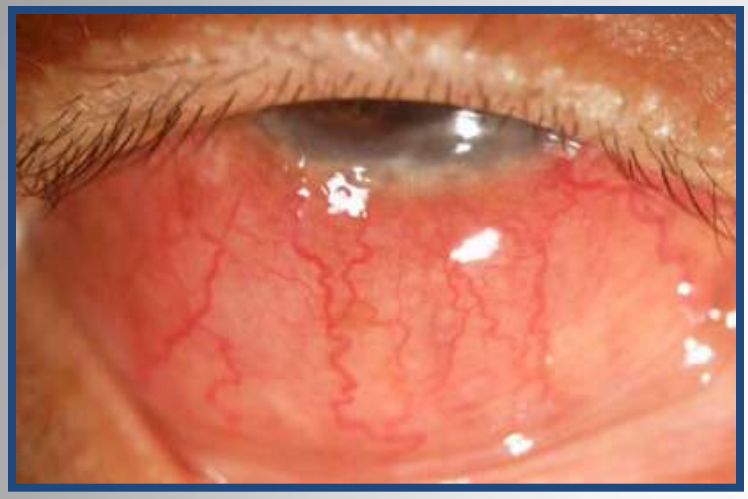


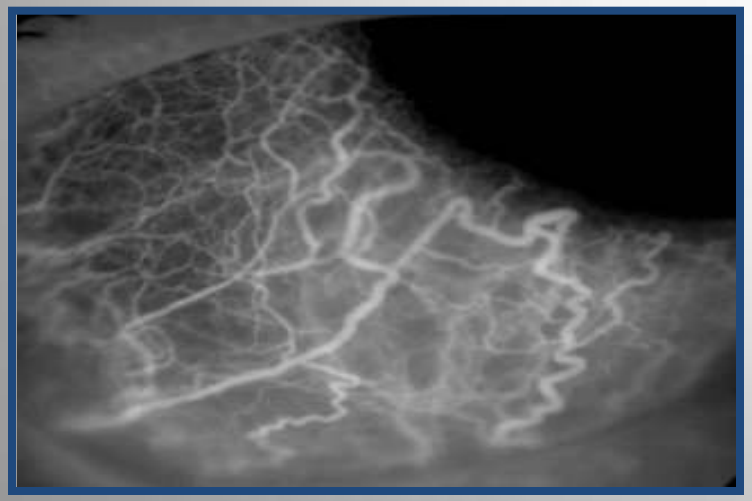
- Nella maggior parte dei casi esordio sclerite è secondario a malattia sistemica
- Prognosi di sclerite legata alla severità della malattia sistemica

Clinica sclerite

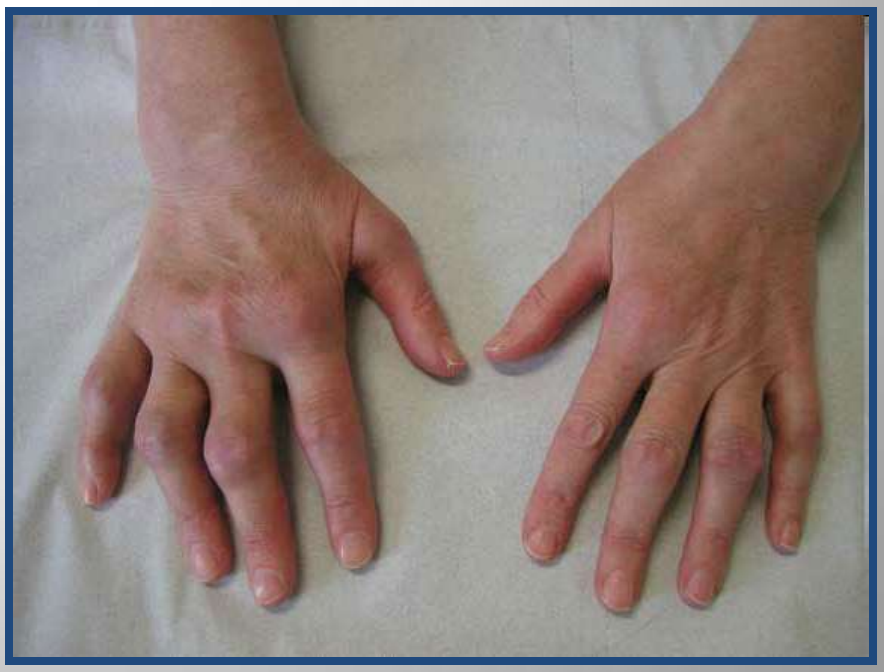
- **Dolore**
- **Arrossamento**
- **Bilateralità**
- **Ricorrenza**
- **Progressione**

Sclerite diffusa

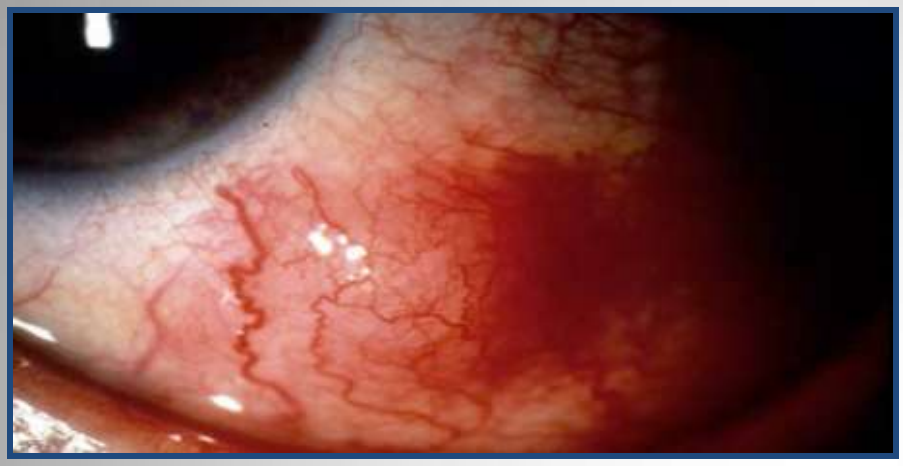


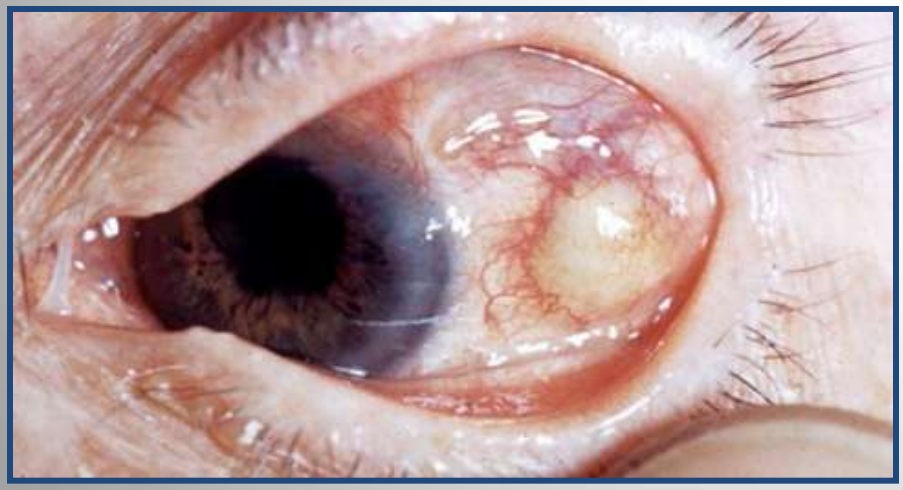


- ✓**Sclerite più benigna e più confusa**
- ✓**Associata nel 45-62% casi a malattie del connettivo (tipicamente artrite reumatoide)**



Sclerite nodulare





Evoluzione a necrotizzante nel 20% casi

Associazione nel 45% a malattie del connettivo (soprattutto artrite reumatoide)

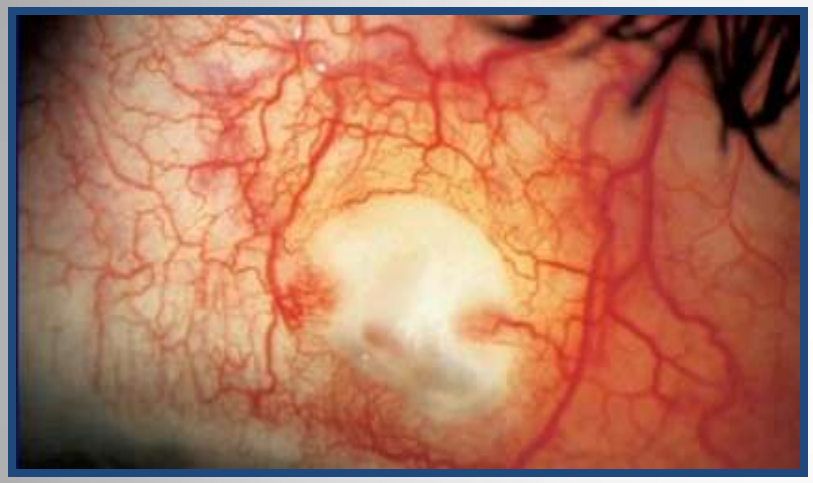
Sclerite necrotizzante

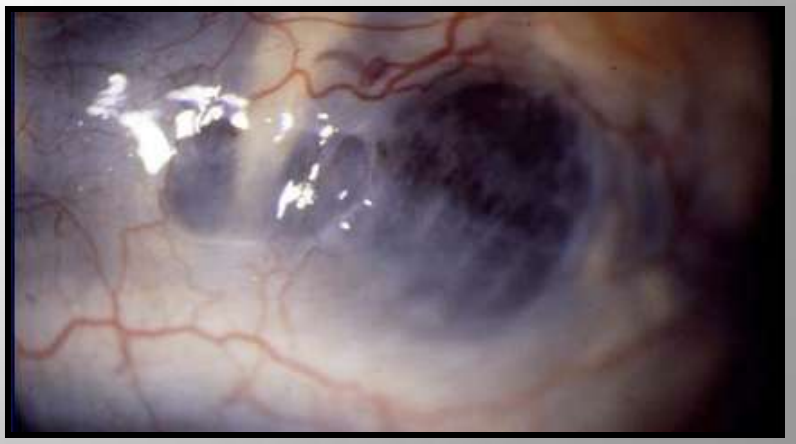
- Con infiammazione
  - Occlusiva venosa
  - SINS (Surgically Induced Necrotising Scleritis)
  - Granulomatosa
- Scleromalacia perforans

Sclerite necrotizzante con infiammazione

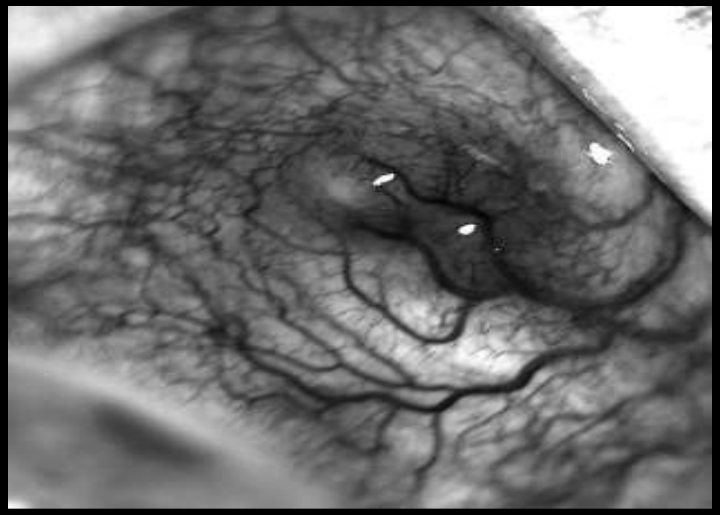
- La più seria e distruttiva
- Rara
- Pazienti anziani >60 anni
- Bilaterale (60% casi)
- Segno quasi patognomonico di malattia sistemica (connettiviti/vasculiti)
- 60-90% sviluppa complicanze oculari (uveite, ulcera corneale periferica, glaucoma, 40% perdita visiva)
- 29% pazienti muore dopo cinque anni dall'esordio della sclerite (soprattutto per lesioni vasculitiche sistemiche)

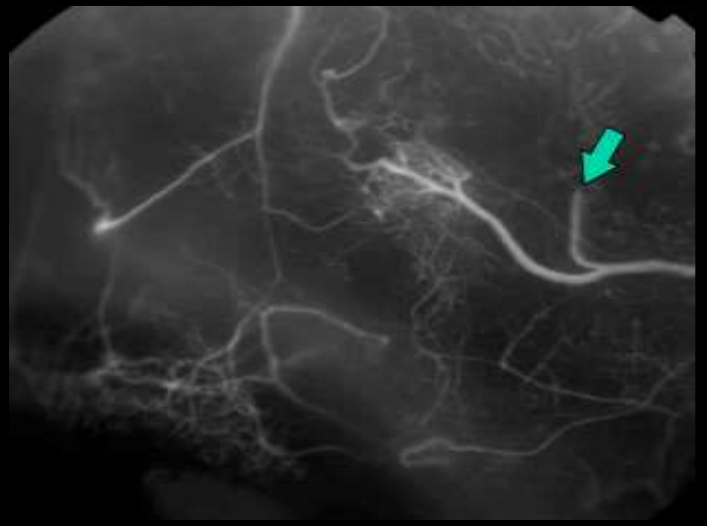
Sclerite necrotizzante occlusiva venosa

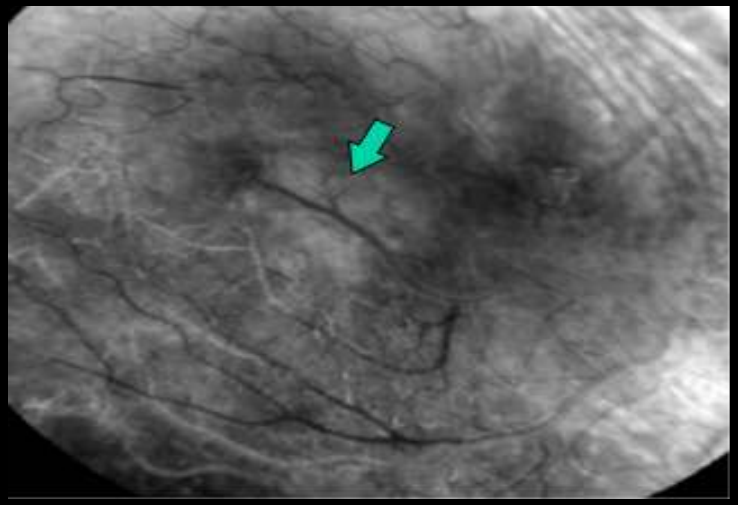


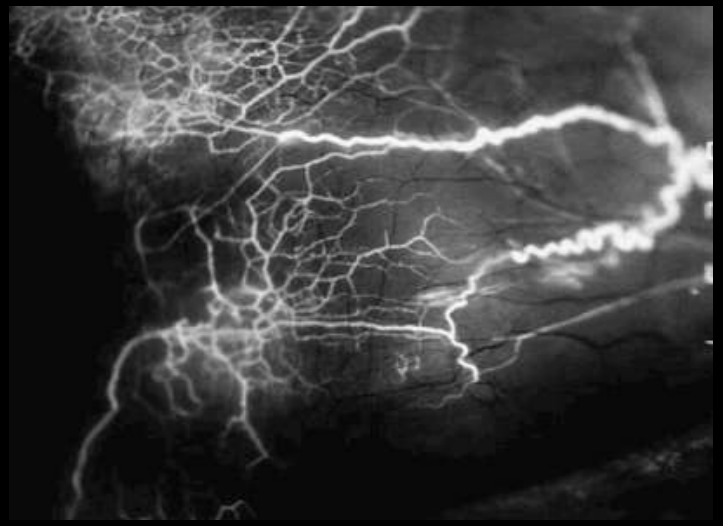


- Dolore intenso, sproporzionato
- Evoluzione in ore/settimane
- Aumento IOP, stafiloma, sclera blu
- **Artrite reumatoide**



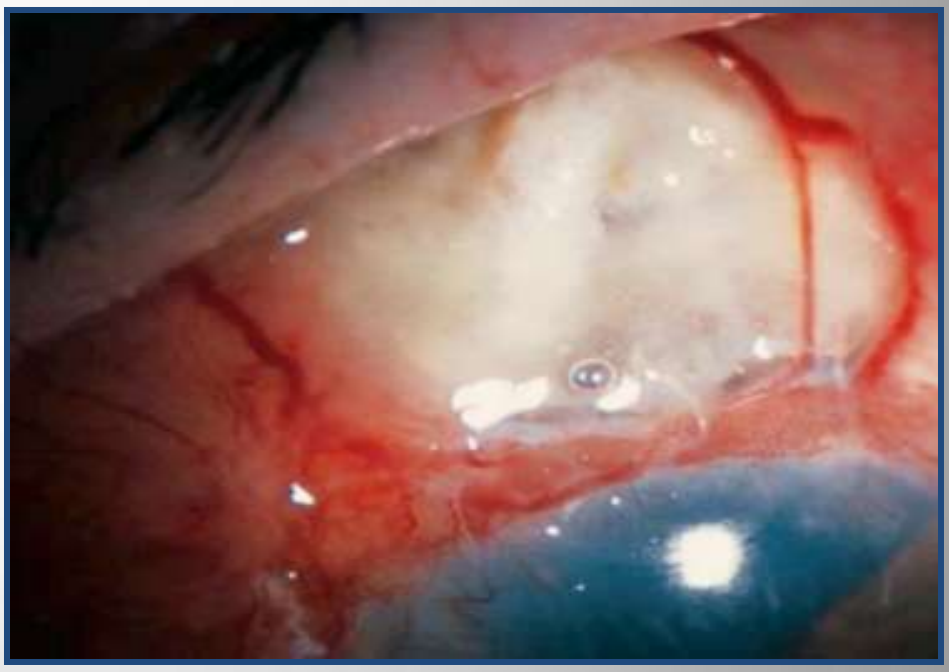






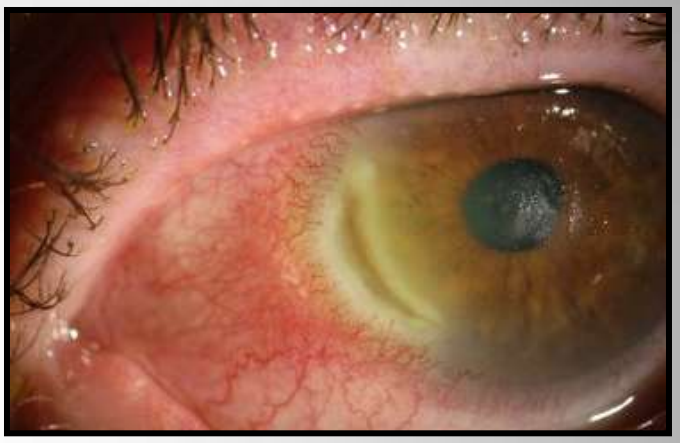
SINS (Surgically Induced Necrotising Scleritis)

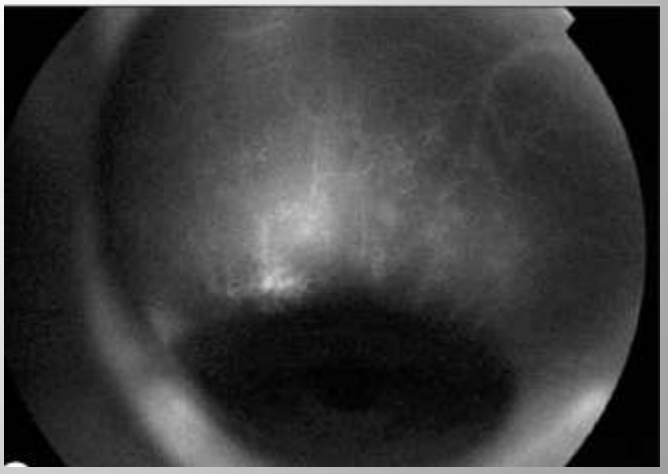
- Esordio entro 3 settimane da un trauma chirurgico:
  - cataratta
  - chirurgia retinica e del glaucoma
  - asportazione di pterigium
- Forte associazione con malattie sistemiche (50-90%)
- Necessaria terapia sistemica anche se assente malattia sistemica



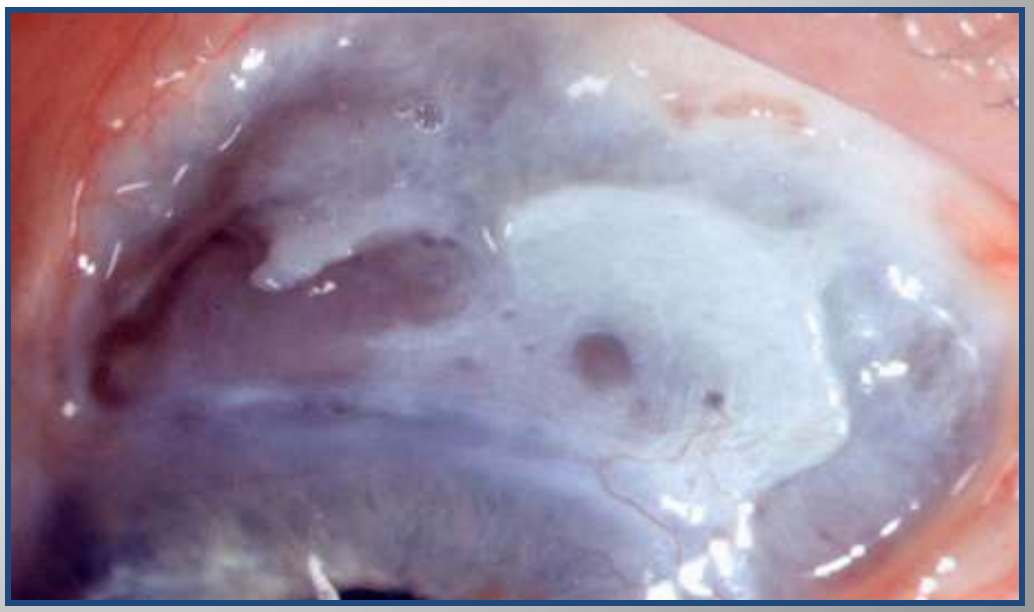
Sclerite necrotizzante granulomatosa

- Arrossamento sclerale perilimbare
- In 24 ore tessuti diventano edematosi
- Progressione all'ulcera/perforazione corneale
- Leakage vascolare, a volte aree avascolari
- **Associazione con:**
  - **Granulomatosi di Wegener**
  - **PAN**





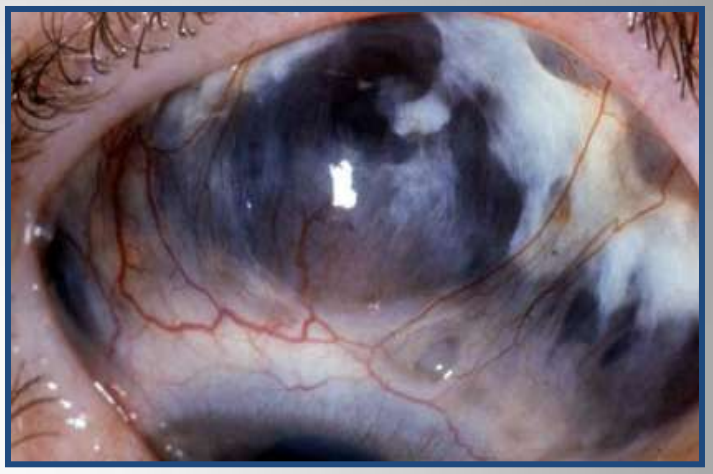
Aprile 2007

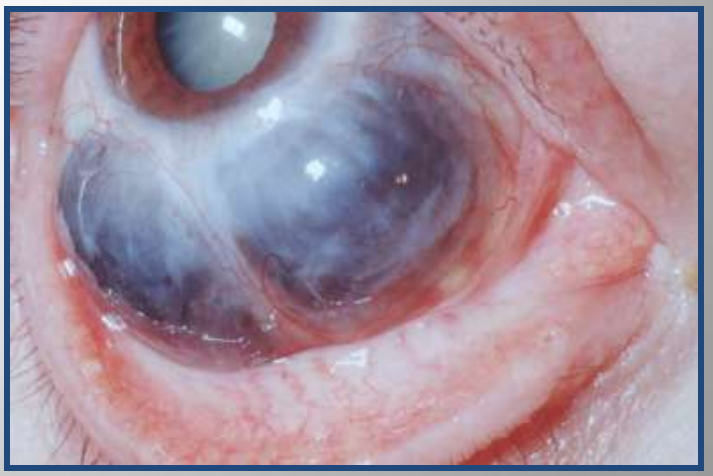


Luglio 2007

Scleromalacia perforante

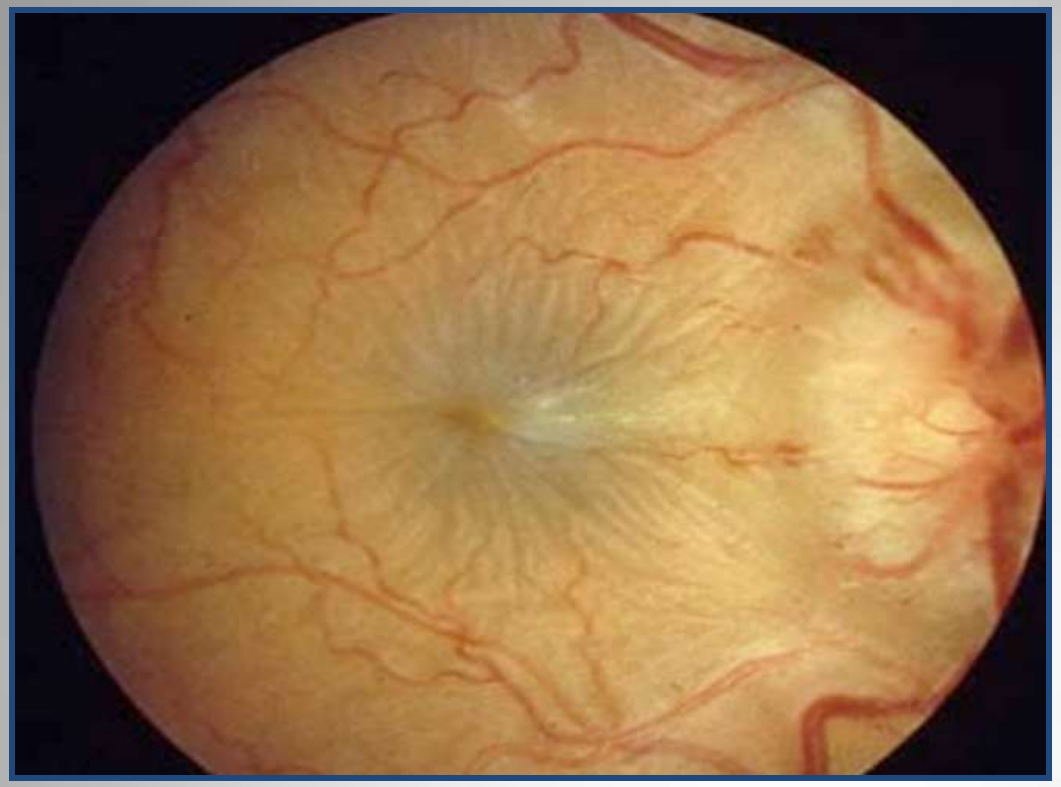
- Scarso dolore
- Età media esordio 70 anni
- Sesso femminile e bilaterale
- **Associazione con artrite reumatoide non attiva (46-67% casi)**
- Placche gialle a circa 3 mm dal limbus
- Rara perforazione spontanea, più frequente rottura traumatica





Sclerite posteriore

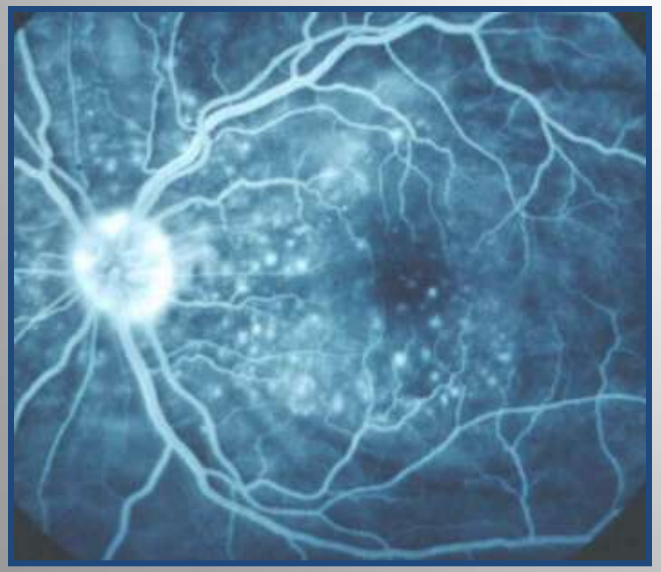
- Incidenza: 2-7.2 % di tutte le scleriti
- Adulti
- Patogenesi:
  - Idiopatica
  - Malattie sistemiche nel 29% dei casi (artrite reumatoide, granulomatosi di Wegener)
- Forme:
  - Diffusa
  - Nodulare
  - Necrotizzante
- Clinica
  - Dolore, associato o meno a segni clinici
  - Perdita visiva variabile

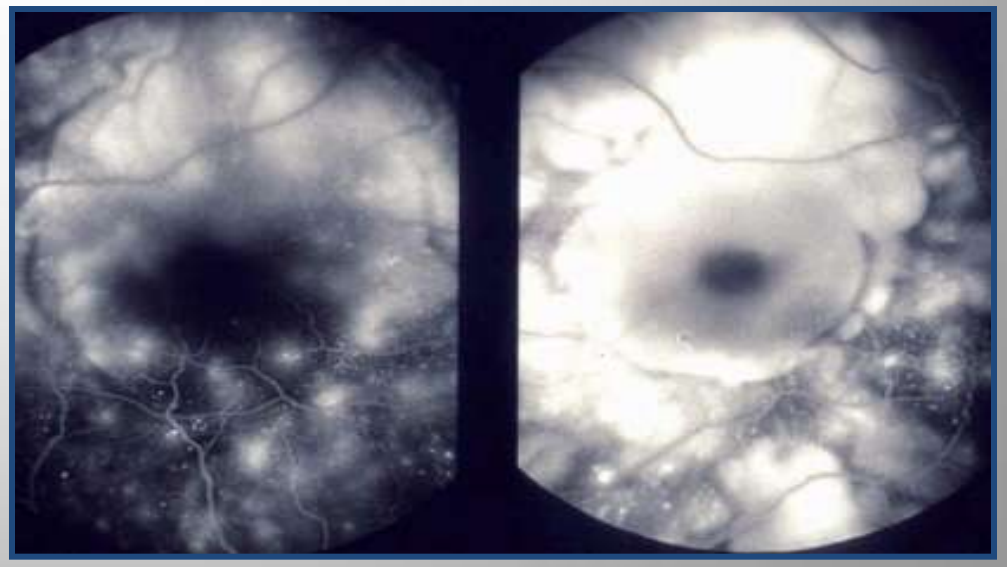


Diagnosi differenziale:

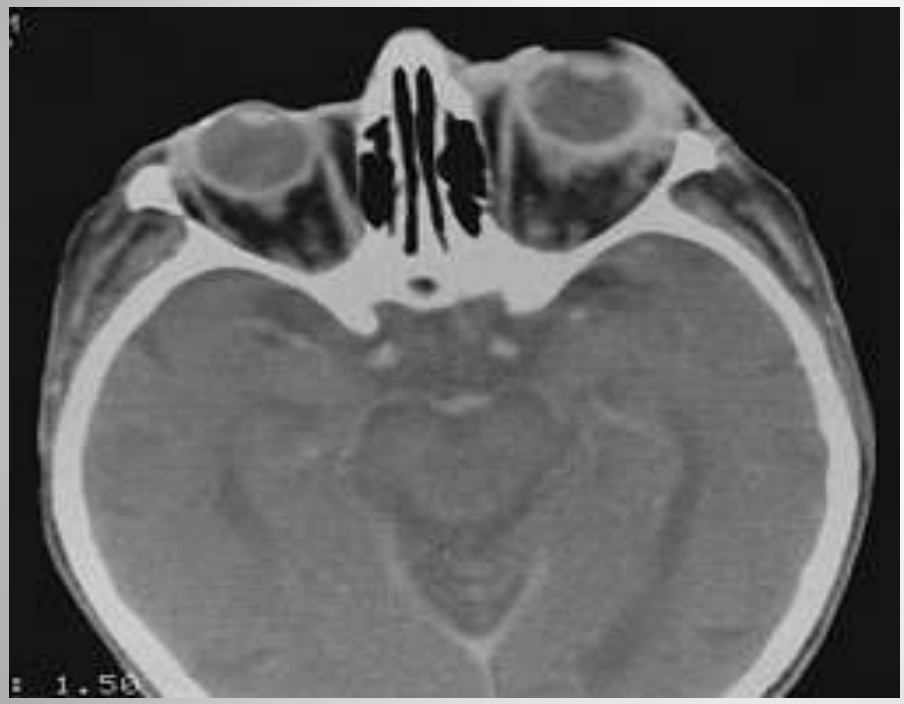
-VKH

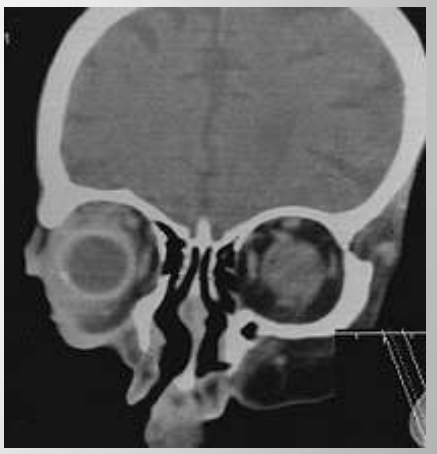
-Distacco corpi ciliari





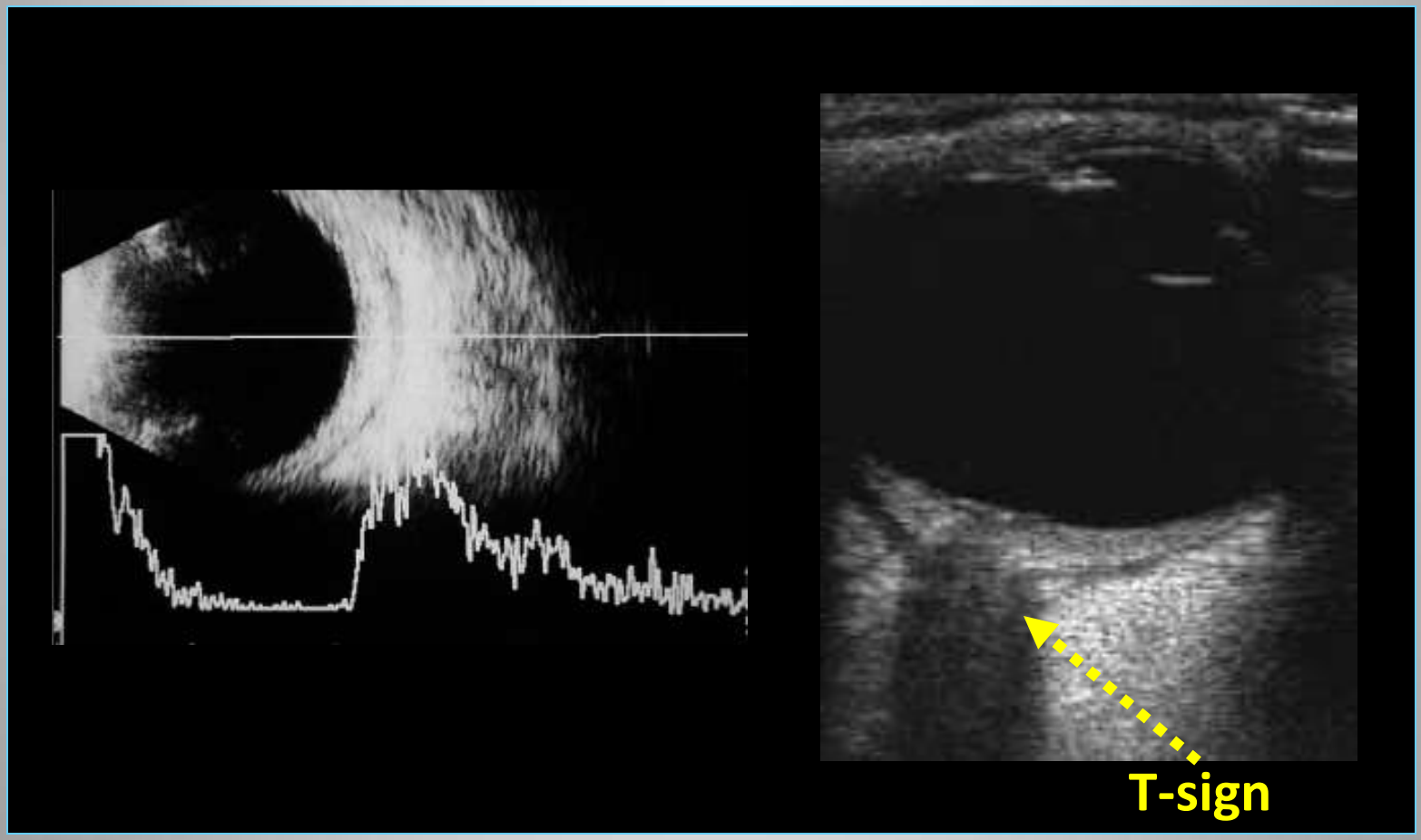
Sclerite posteriore





DD: orbitopatia tiroidea, massa orbitaria, pseudotumor infiammatorio

Diagnosi: US



Work-up scleriti:

Esame chimico-ematologico	Microbiologia	Centro trasfusionale	Altri esami
❑ **Emocromo** ❑ Formula leucocitaria ❑ **PCR** ❑ **VES** ❑ Fibrinogeno ❑ Es. urine ❑ Lupus anticoagulant ❑ ACE ❑ Lisozima	❑ VDRL, FTA-ABS ❑ **FR (WR)** ❑ **ANA** ❑ ENA ❑ AMA ❑ **c-ANCA, p-ANCA** ❑ ASMA ❑ **C3-C4** ❑ Ab Toxo ❑ HIV ❑ Ab Lyme ❑ Ab Brucella ❑ Ab Bartonella	❑ HLA I ❑ HLA II ❑ HLA B27	❑ **PPD** ❑ **Rx torace** ❑ Rx sacro-iliache ❑ RMN encefalo + orb. ❑ Scintigrafia Ga67 ❑ **V. reumatologica** ❑ V. pneumologica ❑ V. neurologica ❑ FAG ❑ ICGA ❑ Ecografia bulbare ❑ UBM

Terapia scleriti:

- FANS:

- **orali: scleriti moderate, non associate a vasculiti**

- Steroidi:

- **<u>orali</u> (in aggiunta o sostituzione ai FANS): prednisone 1 mg/kg/die, a scalare**
- **<u>e.v.</u> (metilprednisolone, 1 gr/die a scalare) in casi di sclerite molto severa e per evitare gli effetti collaterali di terapie orali prolungate**
- **<u>Iniezioni sottocongiuntivali (triamcinolone)</u>: ancora pochi dati in letteratura**

- Farmaci immunosoppressori:

- **Come "steroid-sparing"**
- **Se steroide non efficace**
- **Necessari nelle vasculiti (g. di Wegener, PAN)**

Immunosoppressori:

- **Ciclofosfamide: 1-3 mg/Kg/die**
  - **1° linea per gr. di Wegener e PAN**
- **Methotrexate (+ ac.folico): 7.5-15 mg/settimana x os**
  - **1°scelta come steroid sparing**
  - **Buona tollerabilità ed efficacia**
- **Azatioprina: 1-2 mg/die**
  - **Meno efficace in monoterapia**
- **Ciclosporina: 2.5-5 mg/kg/die**
  - **2° scelta**
- **Micofenolato Mofetil (Cellcept): 1 gr/ 2 volte/die**
  - **Buona efficacia e sicurezza**
  - **Pochi studi**

Biologic Agents in the Management of Inflammatory Eye Diseases

Drug category	Generic name	Trade name	Usual dose in ocular inflammation
A: Drugs targeting:			
Lymphocytes			
B cells	Rituximab	Rituxan (Genentech, South San Francisco, CA)	1 g twice 2 weeks apart IV
All lymphocyte subsets	Alemtuzumab	Campath (Genzyme, Cambridge, MA)	10–12 mg/d for 5 days IV
Proinflammatory cytokines			
Tumor necrosis factor-α	Adalimumab	Humira (Abbott Laboratories, Abbott Park, IL)	40 mg every 2 weeks SC
	Etanercept	Enbrel (Immunex, Thousand Oaks, CA)	50 mg/wk SC
	Infliximab	Remicade (Centocor, Malvern, PA)	3–5 mg/kg every 6–8 weeks IV
Proinflammatory cytokine receptors			
Interleukin-2 receptor	Daclizumab	Zenapax (Hoffman-La Roche, Nutley, NJ)	1 mg/kg every 4 weeks IV
B: Recombinant cytokines:			
Interferons	Interferon-α-2a	Roferon A (Hoffman-La Roche, Nutley, NJ)	3–9 MU/d SC
	Interferon-α-2b	Intron A (Schering, Kenilworth, NJ)	3–9 MU/d SC

IV—intravenous; SC—subcutaneous.

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Studi aperti, non randomizzati!

Piccolo numero di pazienti inclusi!

Chirurgia nelle scleriti

- Patch sclerale