Sarcoidosis
a multisystem chronic inflammation
causing multifocal non-caseating granulomas

BUT – Diagnosis often made indirectly (without histology)

Clinical manifestations can be protean

Limited organ involvement well-recognised
(possibly ocular only)
Aetiology?
Genetic susceptibility – environmental provocateur

• Possible associated micro-organisms:
  – Cell wall-deficient mycobacteria - *MAC, M. paratuberculosis*
  – Propionibacteria - *P.acnes, P.granulosum*
  – Chlamydia trachomatis
  – Human herpesvirus Type 8
  – Rickettsia helvetica

• Seasonal peaks of presentation

• Significant exposure to:
  – Titanium
  – Dust in vegetable processing
  – Sustained high humidity
  – Photocopier toner
Sarcoid uveitis – demographics

- Incidence of sarcoidosis 5:100,000:yr (ocular 25%)
  - Male 1:1.5 female
- Asian 19% (pop 6.5%)
- Black 21% (pop 1.7%)
  - (MUC Figures)
Clinical appearance: anterior

- Characteristically a “granulomatous” uveitis:
  - Large inferior KPs
    - Greasy, mutton-fat
    - Partly confluent
    - Often glueing angle
  - Presentation subacute
  - Eye relatively white
  - Raised IOP frequent
  - PS/PAS frequent
Clinical appearance: anterior

- Iris nodules are infrequent
  - Typically irregular in distribution
  - Typically smallish, sticky
  - Rarely large:
  - If so, sometimes vascularised
The vitreous in sarcoidosis

- 15% of sarcoid uveitis presents as intermediate-type, with large-ish opacities, inferior snowballs +/- snowbanking
- 10% of intermediates diagnosed sarcoidosis
Retinal vasculature

- Intermittent periphlebitis with:
  - exudate
  - tortuosity
  - narrowing
Retinal vasculature

- Macroaneurysm
Retinal vasculature

- Vascular occlusion: uncommon
  - creeping peripheral closedown
  - acute occlusion very uncommon (consider TB)
Choroid and retina

- Typical - multifocal choroiditis
  - Smallish, creamy, moderately-well defined
  - Especially in inferior and nasal fundus, but may be widespread
  - Leave punctate inferior scars which are typical of sarcoidosis
Choroid and retina

- Very uncommon – solitary nodule
Optic nerve head

- Disc or peripapillary granuloma
- Papillitis/neuroretinitis with uveitis
- Papilloedema in neurosarcoid
Systemic involvement

- Syndromes: Löfgren’s, Heerfordt’s
- Pulmonary (<90%) - Hilar/mediastinal nodes, pulmonary infiltrates - interstitial fibrosis
- Neurosarcoid (central>peripheral)
  - Cranial nerves (esp CN V palsy), meningeal
- Skin – Very variable: Lupus pernio, multifocal, ulcerative, pigmented, erythema nodosum
- Myocardial – sudden death
- Arthropathy, lethargy, sweats, weight loss etc
Diagnosing Sarcoidosis - ACE

• Angiotensin Converting Enzyme
  – Produced by endothelial cells in lung, kidney, gonads
  – Normal adult serum levels up to 55 IU/l
  – Normal childhood/adolescent levels up to 75 IU/l

• Secreted by macrophages in sarcoid granulomas
  – Or in Gaucher’s, asbestosis, miliary TB, Hodgkin’s disease etc

• If ACE >100 IU/l, overwhelming likelihood of sarcoidosis

• Beware effect of ACE1/ACE2 inhibitors
  – ? Re-introduce lysozyme estimation
Diagnosing Sarcoidosis - Chest radiography

- **High-resolution chest CT:**
  - Better identification of hilar/subpleural nodes
  - Perivascular micronodules
  - Ground-glass parenchyma
  - Can detect nodes even if CXR reported normal
  - Absence of micronodules/ground glass on HRCT does **not** confirm absence of pulmonary granulomas
Diagnosing Sarcoidosis - Biopsy

- Bronchoalveolar lavage/biopsy
- Mediastinal thoracoscopic biopsy
- Fine-needle liver biopsy – if clinically indicated
- Conjunctival biopsy – directed only
- Skin biopsy – yes!
- Kveim test - historical
Diagnosing Sarcoidosis – Lymphopenia

Manchester Uveitis Clinic
Lymphopenia <1.0x10^9/l in patients with uveitis:

31/117 (26%) patients diagnosed with sarcoidosis
14/328 (4%) patients with other diagnoses
(p=0.0001, RR=5.8)

No evidence of a spurious correlation with:
  ACE level, age at presentation, race
  CXR involvement or systemic severity

Lymphopenia is a simple, independent marker for sarcoidosis in new patients presenting with uveitis

Jones NP et al. 2013
Diagnosing Sarcoidosis – F18,FDG-PET

- F18, fluorodeoxyglucose Positron Emission Tomography
- Preferential take-up by rapidly metabolising cells
- Extensively used for oncological tumour mapping
- Also identifies occult inflammation in sarcoidosis
  - especially extrapulmonary, especially where ACE normal
  - may facilitate guided biopsy to confirm diagnosis
Diagnosing Sarcoidosis - others

• Calcium metabolism
  – Sarcoid granulomas secrete vitamin D but:
    • only 10% have hypercalcaemia
    • only 2% are symptomatic
  – $\text{Ca}^{++}$ raised, $\text{PO}_4^-\ N$, Phosphatase sl raised
  – 24-hr urinary Calcium raised

• Anergy – failure of Type IV hypersensitivity
  – Antigens: Tuberculoprotein, tetanus toxoid, Candida antigen, mumps virus
  – Possibly abnormal dendritic cell response
NPJ diagnosis/referral

• “Qualifying” uveitis:
  – ACE
  – CXR: if equivocal, or if normal with raised ACE - HRCT
  – Liver & kidney function
  – Biopsy easily-accessible skin/conj lesions
  – Abnormal CXR or systemic symptoms – physician referral for:
    • Baseline lung function
    • Bronchoscopy + lavage ? Biopsy
  – Exclude TB if risk identified from patient history
Treating sarcoidosis

- There are no aspects of ocular sarcoidosis which are disease-specific; general principles of uveitis treatment

- Almost all are steroid-responsive
  - if resistant – reconsider TB

- Depot/intraocular steroid for macular oedema

- Immunosuppression - sometimes

- Anti-TNF alpha?
  - Infliximab highly effective for severe pulmonary disease (but exclude TB!)

- Hydroxychloroquine for skin involvement
To conclude:

- A common cause of uveitis in Western world
- Most patients with uveitis present because of it:
  - Later development is unusual
  - Screening for ocular disease? – little evidence
- Liaison with physicians - control dosage of drugs
- Only rarely a blinding disease
All the files listed below have been made available by the author in fully editable format for adaptation and use in clinical practice.

Management protocols
- Acute Anterior Uveitis
- Unilateral
- Aqueous Sampling
- Azathioprine
- Bevacizumab
- Intraocular
- Cardiovascular Disease in the Uveitis Clinic
- Cataract Surgery
- Ciclosporin
- Ganciclovir - Intraocular
- Health Review Form
- Instructions
- Health Review Form

Patient information pamphlets
- Methotrexate
- Methylprednisolone
- Intravenous
- Mycophenolate Mofetil
- Prednisolone
- Sarcoidosis
- Diagnosis
- Tacrolimus
- Toxoplasmosis
- Triamcinolone
- Intraocular
- Varicella-Zoster Virus
- Viral Retinitis
- Anti TNF alpha
- Azathioprine
- Behçet’s Disease
- Birdshot Retinopathy
- Cataract
- Ciclosporin
- Fuchs’ Heterochromic Uveitis
- Glaucoma
- HLA-B27
- Immunosuppression, Vaccination and Travel Abroad
- Intermediate Uveitis
- Juvenile Idiopathic Arthritis Screening
- Macular Oedema
- Methotrexate
- Mycophenolate Mofetil
- New Patient Questionnaire
- Prednisolone
- Sarcoidosis
- Tacrolimus
- Toxoplasmosis
- Triamcinolone
- Intraocular
- Uveitis
- Viral Retinitis
- Vitrectomy