Sarcoidosis

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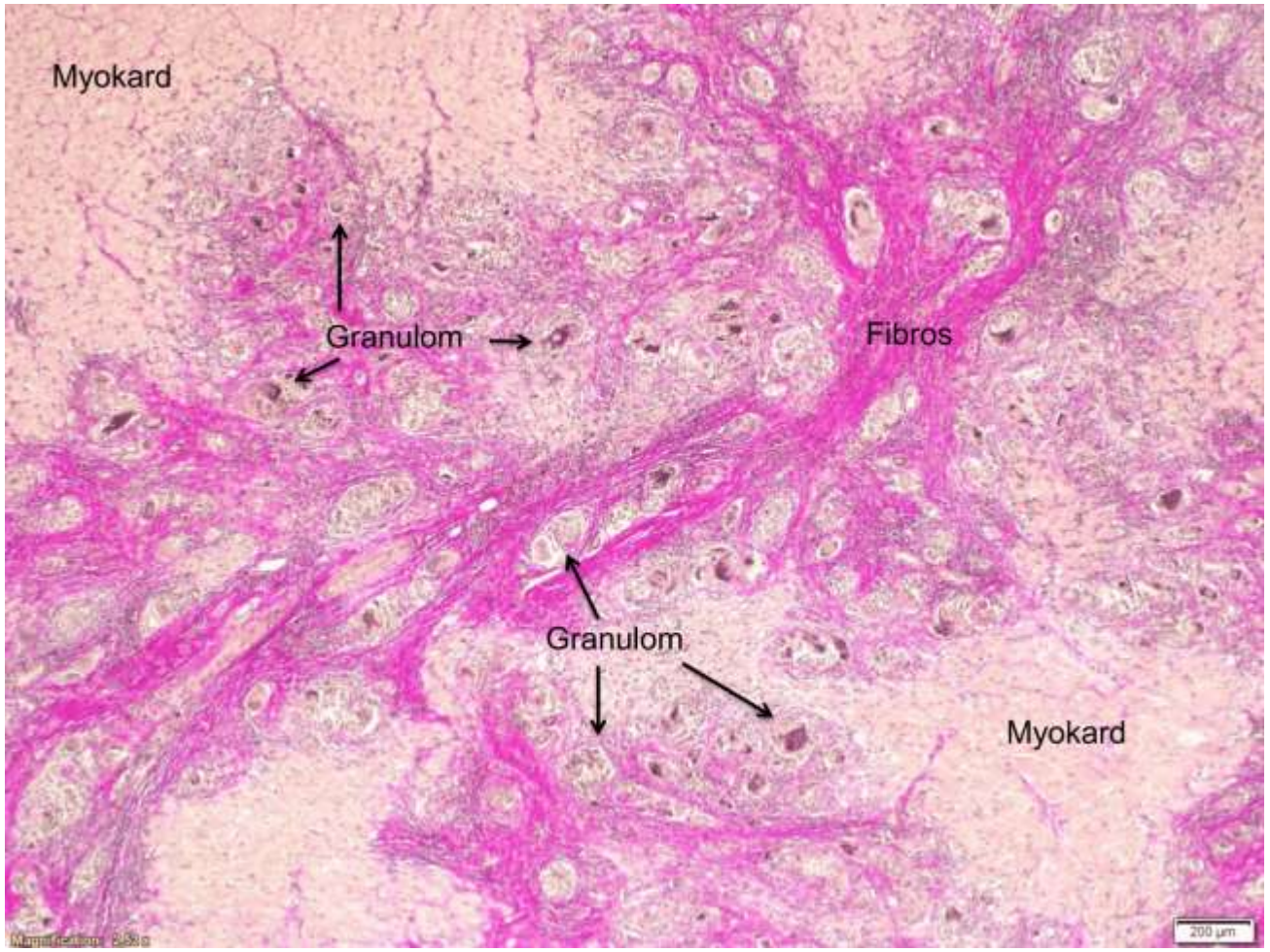
Case

- Female; 64 yrs
- Medical history

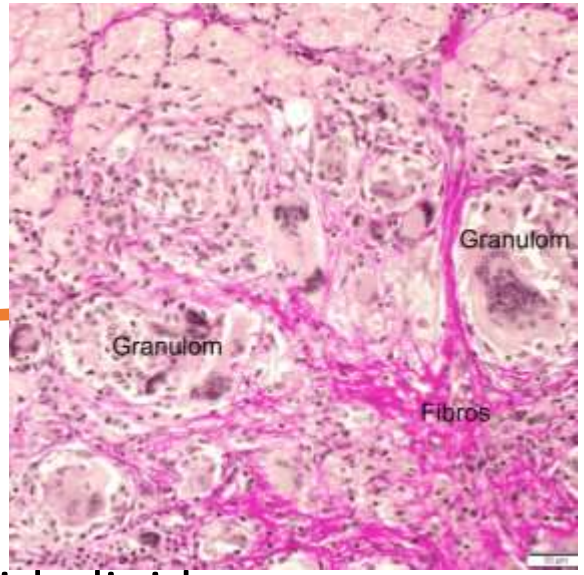
- Op malign thymom. Cytostatics (*10CHOP – low doxorubicin*).
- Polymyosit
- 2002 MALT lymphoma (*radiation therapy*). Recidiv 2004 (*radiation therapy*)
- Sjögren Syndrom (*Mabthera treatment 2010-2016*)
- 2013 – AV block II-III. Permanent PM (Echocardiography- Normal findings)
- 2016 – Heart failure
- Echo- Bi ventricular HF (LV/EF 20% ; Dilated RV, Severe TI); CPET: VO2 max 9ml/kg/min
- MRI ej possible due to MRI incompatible PM
- 2018 – referring for heart transplantation

DIAGNOSIS: Cytostatic induced CMP

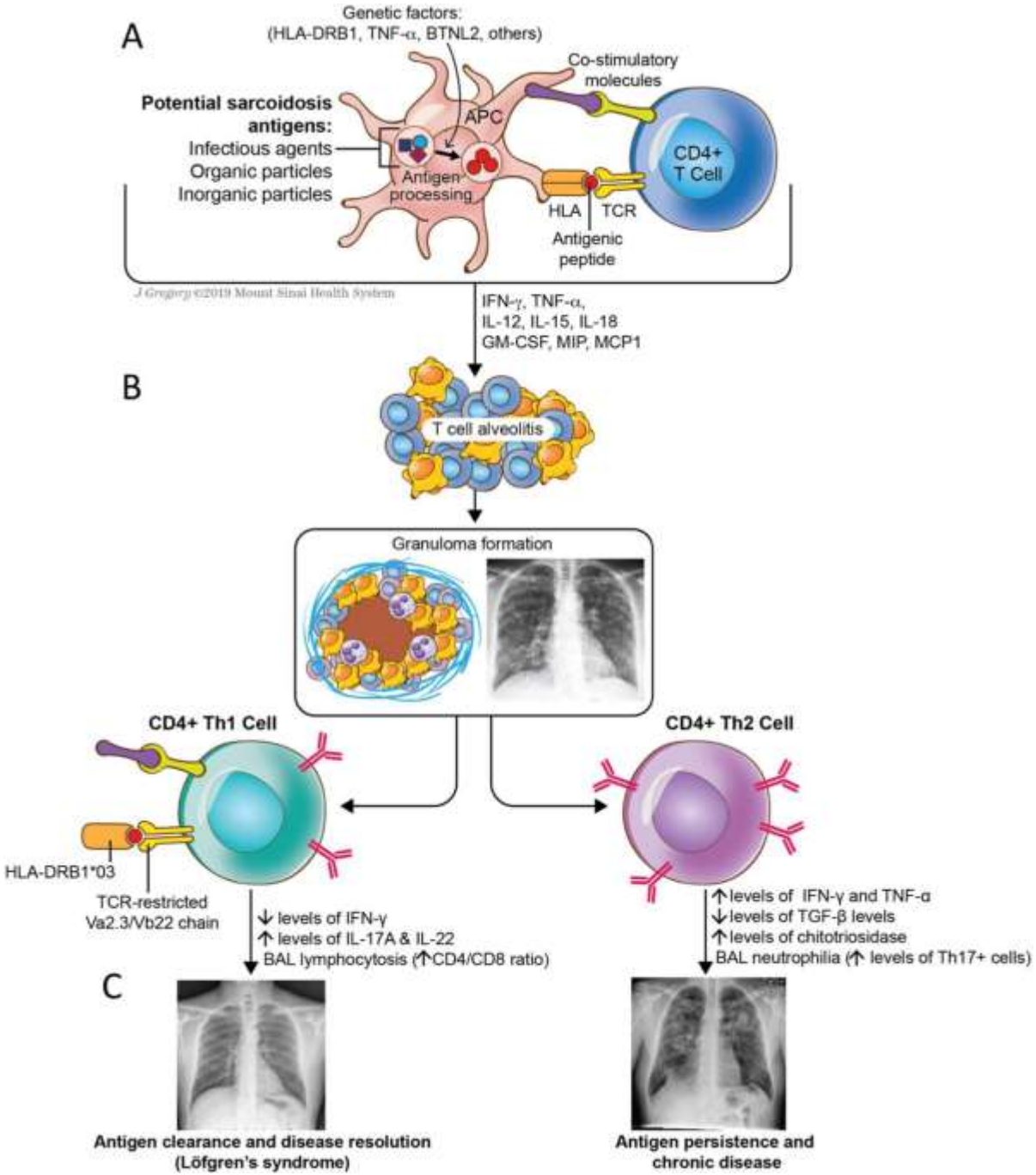
Explanted heart



Sarcoidosis



- Hallmark is non-caseating granulomas, composed of a central core of epithelioid histocytes and multinucleated giant cells
- Activated T cells and macrophages accumulated at site of inflammation
- Release chemo attractants and GF's lead to cellular proliferation and granuloma formation
- Progressive granulomatous inflammation lead to injury, dysfunction and destruction of the affected organs



- Cause is unknown, both genetic and environmental factors suspected

- Theory: *Disease develops un genetically pretermined host who are exposed to certain environmental agents that trigger an exaggerated inflammatory immune response granuloma formation*

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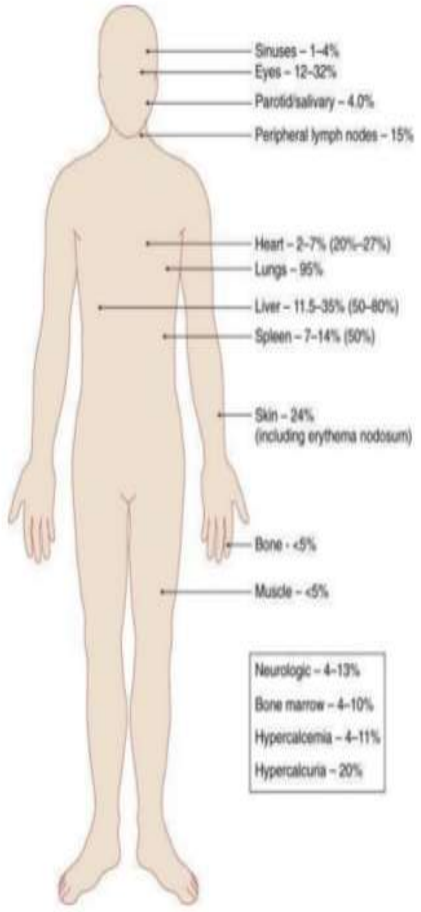
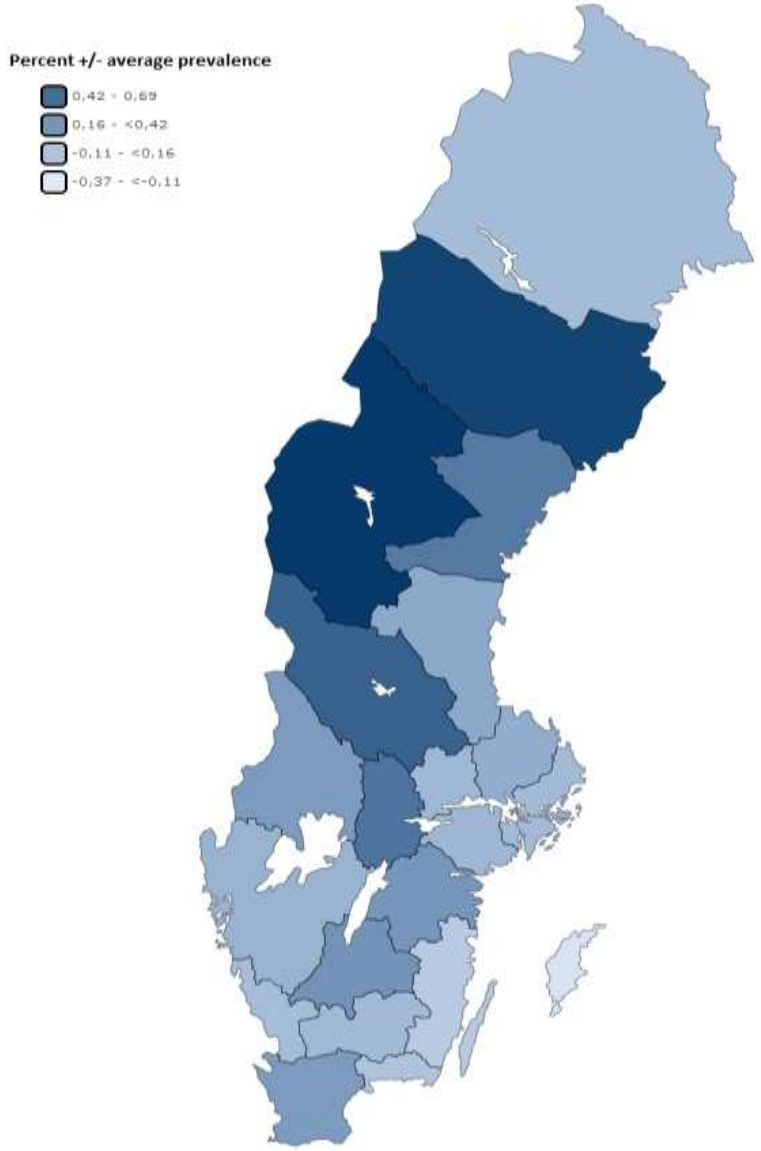
	Systems affected by Sarcoidosis Sign and Symptoms
Cardiac	• Palpitations, syncope, chest pain, arrhythmia, sudden death
Cutaneous	• Erythema nodosum, plaques, subcutaneous nodules, alopecia, hyper/hypopigmentation
Endocrine	• Hypo/hyperthyroidism, adrenal insufficieincy
Exocrine	• Painless sweelling of parotid gland, kerato-junctivis sicca
Hepatic	• Asymptomatic or abdomina pain, abnormal LFTs, hepatomegali
Lymphatic	• Extrapulmonary lymphadenopathy, spelonemegaly





Totalt 16000

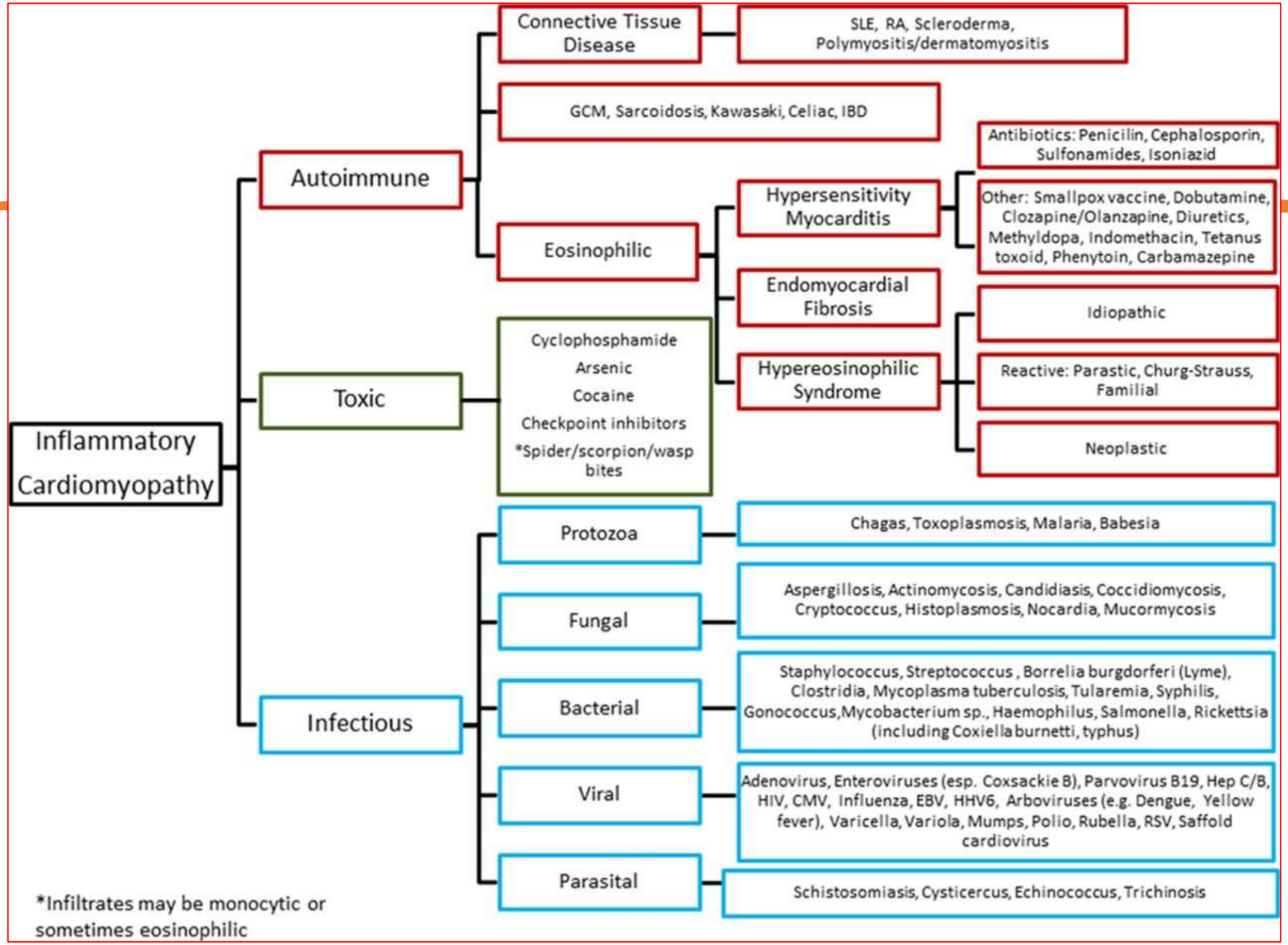
50 år

55% män

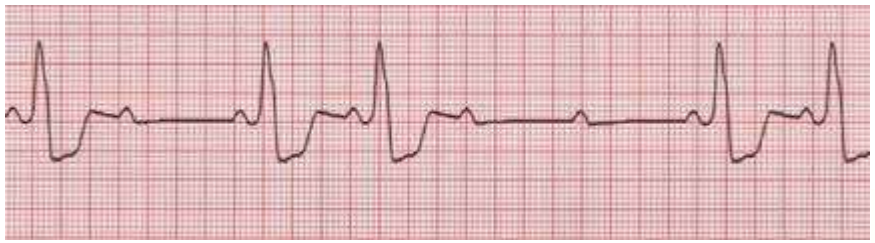
90%

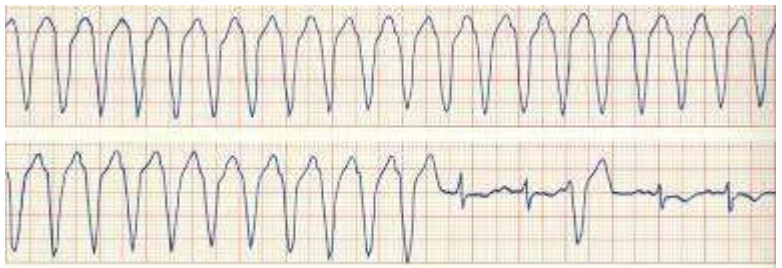
5-(25)%

Sarcoidosis incidence and prevalence: a nationwide register-based assessment in Sweden
Elizabeth V. Arkema, Johan Grunewald, Susanna Kullberg, Anders Eklund, Johan Askling
European Respiratory Journal Dec 2016, 48 (6) 16901699; **DOI:** 10.1183/13993003.00477-2016



Circ Res 2017; 121: 803-818,





Other signs

Atrial Fibrillation? Aneurysm? Stroke?
Diastolisk heart failure
Coronary arteries granulom/ischemia?

Non-invasive diagnostics

Early stage

- Signs of inflammation? Grade? Heart? Other organs?
- Inflammation? Fibrosis? Where and How much ? Left ventricle/right ventricle?

Relation between – clinical finding/MRI/PET/CT

Chronic stage

Re-Evaluation

- Under treatment
- After treatment
- Recurrence

Sammanfattning

- Potentiellt allvarligt sjukdomstillstånd, ffa hjärtsvikt, AVB och VT/VF
- Klinisk manifest sjukdom hos 5% av sarkoidospat
- Ofta hjärtat som är första symptomet
- Samarbete multidisciplinärt, inte någon enkel diagnostik
- Långvarig behandling, inte sällan kombinationsbeh
- Följ pat under beh, tidigt efter beh och minst 3-5 år efter avslutad beh
- Samarbete klinik och forskning både nationellt och internationellt behövs

Heart Rhythm Society Criteria for the Diagnosis of Cardiac Sarcoidosis

Histologic diagnosis - Definite	**Clinical diagnosis - Probable**
Positive endomyocardial biopsy (noncaseating granulomas) without alternative aetiology	**Biopsy-proven extra-cardiac sarcoid and ≥ 1 of the following:** • Steroid/immunosuppressant-responsive cardiomyopathy or heart block • Unexplained left ventricular ejection fraction < 40% • Unexplained sustained (spontaneous or induced) VT • 2^{nd} (type II) or 3^{rd} degree heart block • Patchy uptake on cardiac PET (in a pattern consistent with cardiac sarcoidosis) • Delayed enhancement on CMR (in a pattern consistent with cardiac sarcoidosis) • Positive ^{67}Ga uptake (in a pattern consistent with cardiac sarcoidosis) Furthermore, other causes for the cardiac manifestation(s) have been reasonably excluded.

Screening for patients without diagnosed sarcoidosis

(medical history, ECG, ultrasound, coronaryangiography)

Type II AV-block or AV Block III (age <60år)
Non-sustained VT
Unclear cause to heart failure?

Contraindication for Cardiac MRI?

Nej

Ja

Low probability for cardiac sarcoidosis

Pathological findings on MRI

Ja

^{18} F –FDG PET
Pathological FDG uptake in myocardium and/or in other organs?

Ja

Image guided biopsi
(myocardium or/and other organs

Other causes? Re-evaluation?

Hittadokument.vgregion.se/hjärtsarkoidosis

Screening for patients with verified sarcoidosis in other organs

(medical history, ECG, Ultrasound, Holter ECG)

Type II AV-block eller AV Block III (age <60år)
Non-sustained VT
Unclear cause to heart failure?

Nej

Monitoring
Reevaluation if new symptoms, ECG

Ja

Contraindikation for MR heart?

Nej

Pathological findings on Cardiac MRI-heart

Nej

Low probability for cardiac sarcoidosis

Ja

^{18} F –FDG PET
Evaluation of degree of inflamation before start with Prednisolone

Ja

Endomyocardial biopsy

Ja

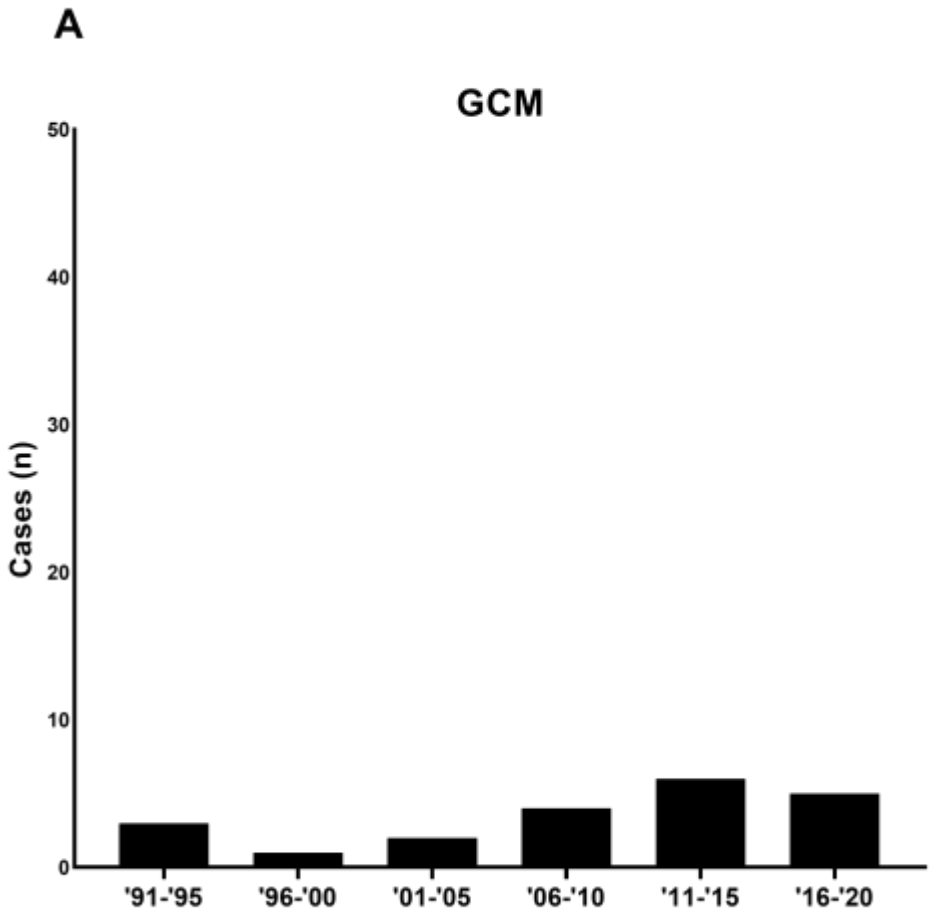
^{18} F –FDG PET
Pathological FDG uptake in myocardium?

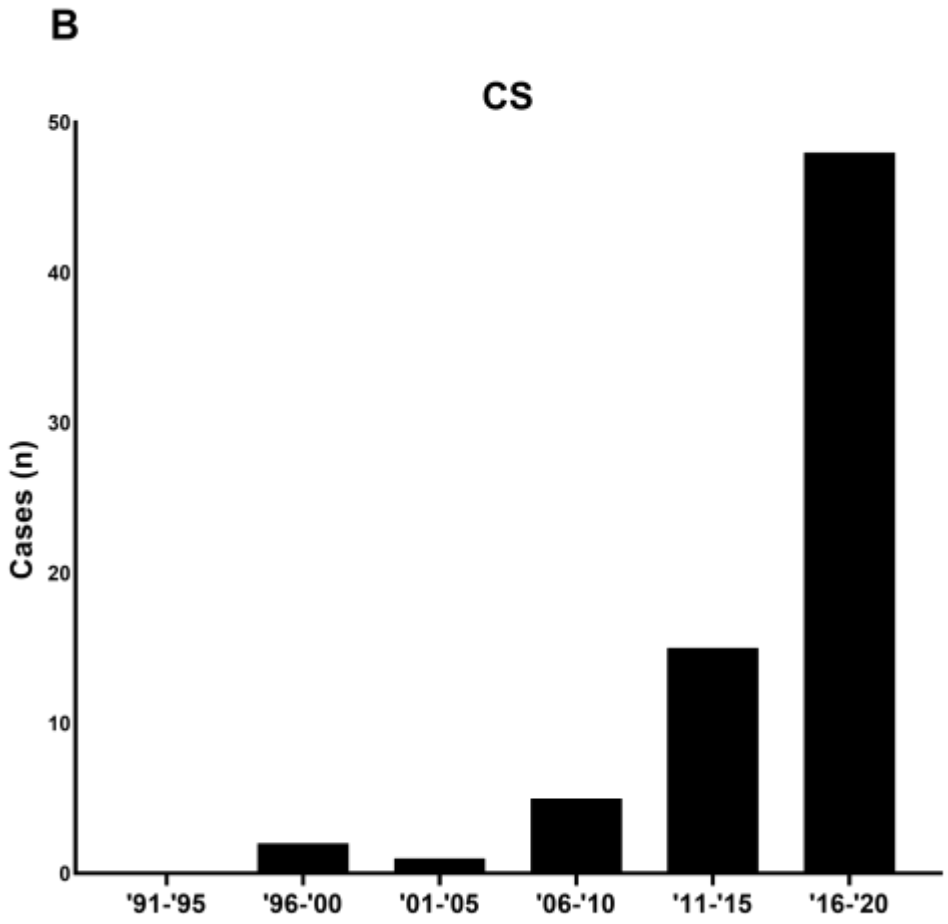
Ja

Other causes? Re-evaluation?

Nej

Sahlgrenska Sjukhuset





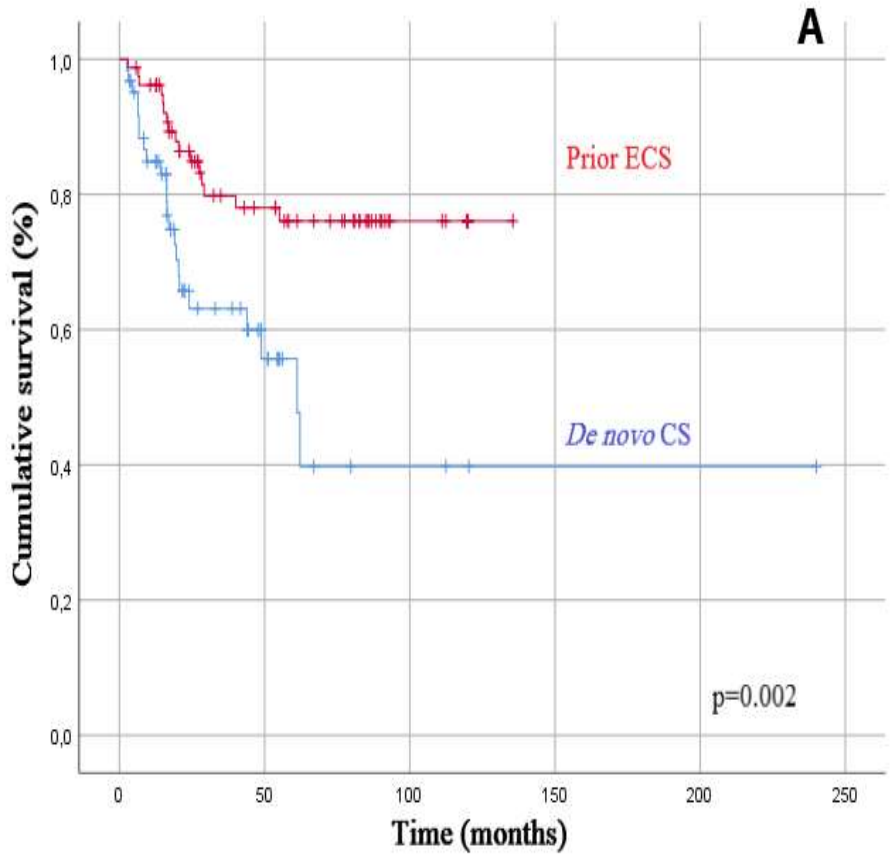
Clinical Outcomes and Predictors of Long-Term Survival in Patients With and Without Extra-Cardiac Sarcoidosis:A Swedish Multicenter Study

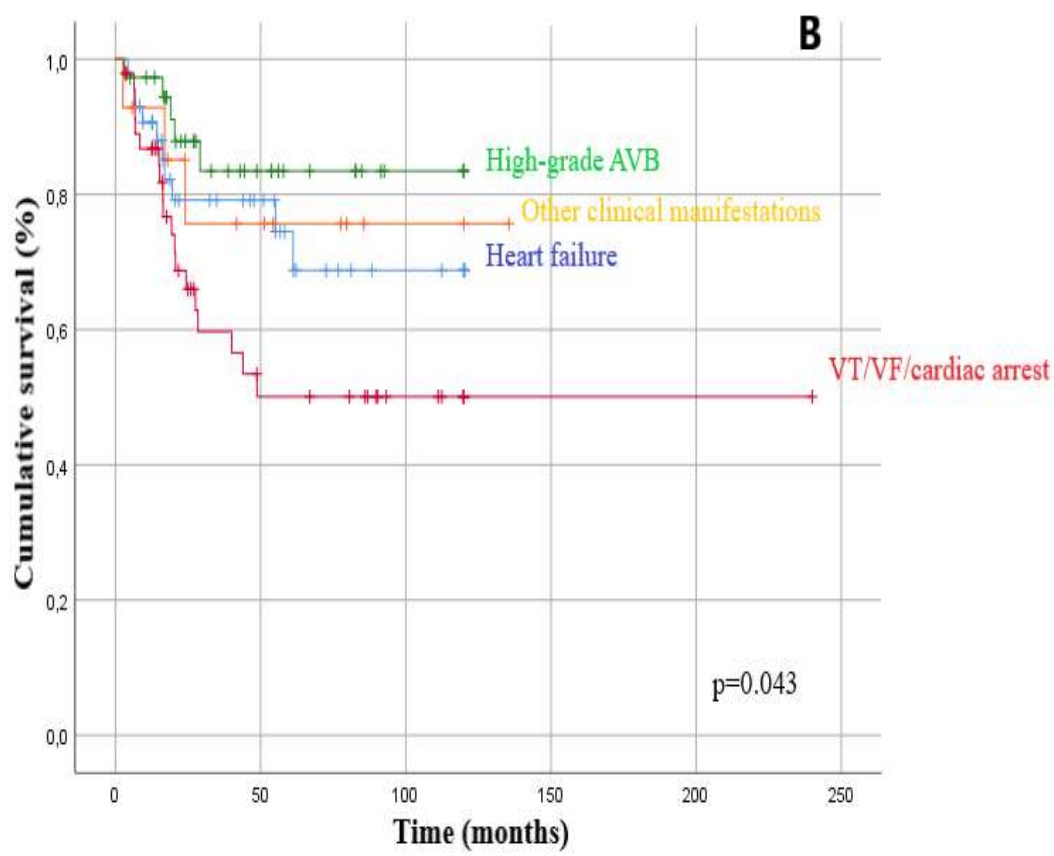
E. Bobbio[1]; P. Eldhagen[2]; C.L. Polte[1]; C. Hjalmarsson[1]; S. Kullberg [2]; P. Sorensson[2]; N. Bergh[1]; E. Bollano[1]

[1]Sahlgrenska Academy, Institute of Medicine, Gothenburg, Sweden;
[2] Karolinska University Hospital, Stockholm, Sweden

Table 1. Clinical and demographic characteristics of the whole study cohort and patients with *de novo* CS and prior ECS

	Entire cohort (N=141)	*De novo* CS (N=62)	Prior ECS (N=79)	*p*
Demographic characteristics				
Age (years)	53 (47-59)	54 (48-60)	53 (47-57)	0.435
Sex (female)	45 (32)	18 (30)	27 (34)	0.735
BMI (kg/m^2)	26.8 (24.1-30.1)	27.8 (25-30.6)	25.9 (23-29.1)	0.032
NYHA ≥ III	39 (28)	25 (42)	14 (18)	0.02
Lab				
NT-proBNP (pg/mL)	823 (235-2441)	2,367 (772-5,400)	335 (128-1,027)	<0.001
Troponin T (ng/L)	28 (12-59)	55 (29-73)	15 (7-30)	<0.001
s-Creatinine (mg/dL)	88 (77-103)	94 (80-114)	86 (73-99)	0.036
Echocardiography				
LVEF (%)	50 (35-55)	45 (30-55)	53 (36-57)	0.052
LVED diameter (mm)	56 (50-62)	56 (51-63)	56 (49-62)	0.316
LV DD	43 (41)	19 (39)	24 (44)	0.762
RV dysfunction	39 (34)	27 (53)	12 (19)	<0.001

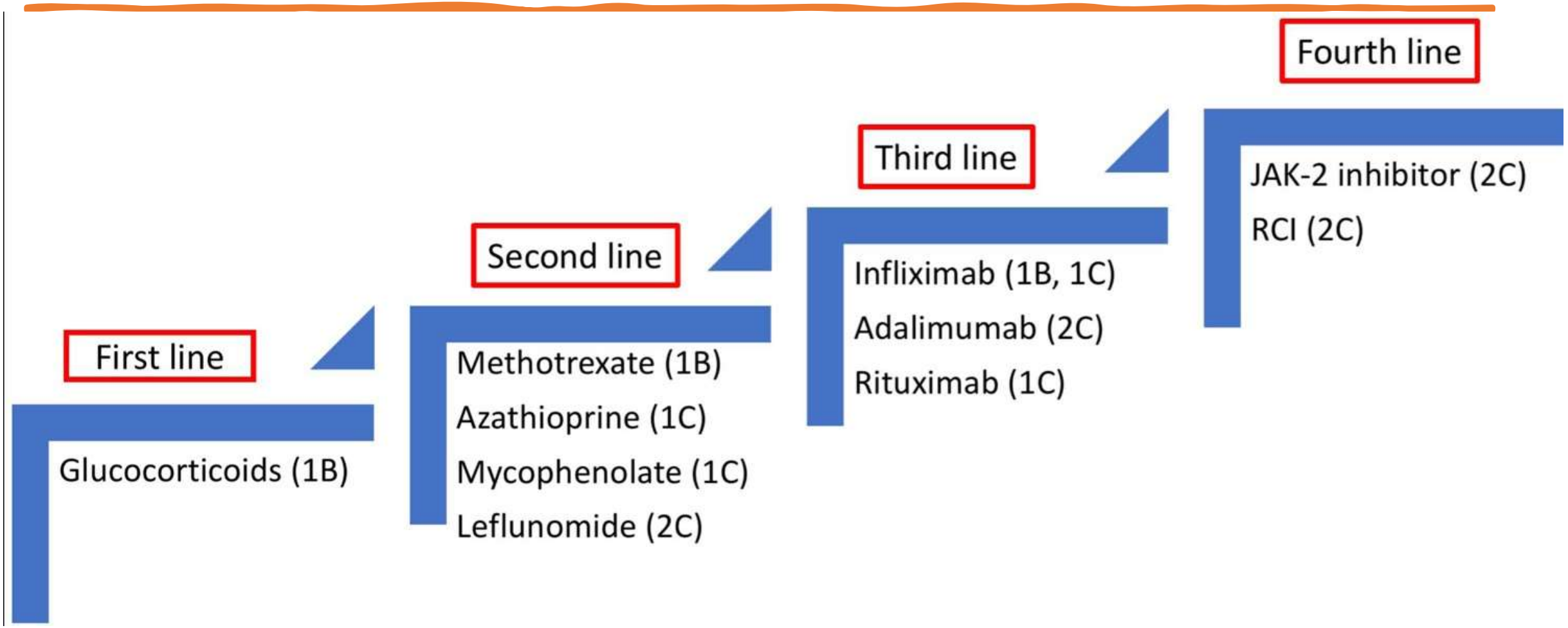

A
Cumulative survival (%)
1,0
0,8
0,6
0,4
0,2
0,0
0
50
100
150
200
250
Time (months)
Prior ECS
De novo CS
p=0.002


B
Cumulative survival (%)
1,0
0,8
0,6
0,4
0,2
0,0
0
50
100
150
200
250
Time (months)
High-grade AVB
Other clinical manifestations
Heart failure
VT/VF/cardiac arrest
p=0.043

Treatment

- Prednisolon
- Metothrexate
- Azatioprim (ImureL)
- Cell Cept
- TNF alfa inhibtors (i.v)

- Heart failure treatment
- Antiarytmics (*Sotalol, Cordarone..)*
- Ev Ablation
- PM/ICD



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Diagnostic algorithm

No prior history of Sarcoidosis

- ✓ Advanced AV block
- ✓ Sustained VT
- ✓ Unexplained systolic or diastolic HF

Biopsy proven extra-cardiac sarcoidosis

- ✓ Symptoms/history
- ✓ Abnormal ECG/Holter
- ✓ Abnormal Echocardiography